

are permanent. The operation of anterior rhizotomy was performed as far back as 1933, but was unsuccessful, mainly because of failure to identify the correct nerve roots; however, it is now an accepted surgical attack on the problem, and is favoured in America (Munro, 1952). At Stoke Mandeville, England, the more conservative method of intrathecal alcohol block is favoured (Guttmann, 1957).

The surgical methods of treatment can be applied only where the paralysis is total and permanent; but there are many patients who have such a degree of voluntary control that if the spasms could be controlled they would be able to perform many useful functions. It is because of this problem that the pharmacological approach is most important.

Pharmacological methods of controlling spasms have not been very successful, although experimental evidence has often been encouraging. Barbiturates do not have any effect on paraplegic spasms, and even at sufficient doses to produce surgical anaesthesia the action on the brain and that on the spinal cord differ. Barbiturates will inhibit the spontaneous activity of the cortex, but will not inhibit afferent stimuli from reaching the cortex. They appear to function merely as a central nervous depressant at a cortical level (Goodman and Gilman, 1941). Berger and Bradley (1946) published their report on mephenesin, which, in small doses, produced depression of the reflex excitability of the spinal cord, and this was shown to exert a selective action on the spinal cord as well as to possess lissive power—that is, it has a selective inhibition of pathological rigidities without diminution of voluntary power. A drug will relieve spasticity if it substantially diminishes the total facilitatory impulses, even though the residue of inhibition is likewise diminished. Heneman, Kaplan and Unna (1949) showed that mephenesin established a new balance at a lower level of activity, and that the most likely site of action was the internuncial neurone. However, they point out that while pharmacologically it had considerable importance, clinically it was disappointing, and this has also been our experience with the drug.

Kahn and Bickers (1948) attempted to use curare as a means of controlling spasms, and they state that no beneficial effects relating to the relief of spasms in paraplegics or paraparetics were obtained by the intramuscular injection of d-tubocurarine in oil. A double-blind test was introduced by these authors, and their comment that "the role of suggestibility in therapy was clearly demonstrated" has been borne out by our experience with this compound.

In 1955 a report on the use of chlorpromazine to control spasms was published by Basmajian and Szatmari. These authors found a dramatic abolition of spasticity for about two hours in four paraplegics. Eleven patients with cerebral palsy and choreoathetosis and one patient with Parkinsonism were also treated with varying results. Residual muscular activity was not further depressed except in one patient, who had transient paralysis. However, evidence on the action of chlorpromazine has been contradictory, and Wislicki (1958) showed in experimental animals that the intraarterial administration of chlorpromazine caused an irreversible neuromuscular block, and that intravenous injection produced a neuromuscular block only in a muscle which was fatigued and stimulated at high rates.

Zoxazolamine ("Flexin") was studied and compared with other muscle relaxants, and its use in conditions of spinal spasticity was attempted by Krantz and Carr (1958). However, clinical evaluation has shown no evidence of lessened spasticity of skeletal muscle after a therapeutic trial on paraplegic patients (Weiss, D'Orozzo and Ebel, 1957). Methocarbamol ("Robaxin") has been shown to have a prolonged depressant effect on the multisynaptic reflexes of the spinal cord, but the drug has yet to be fully evaluated clinically.

In 1957 tigloidine hydrobromide was tried and found to be strikingly successful in the control of spasms. In

this paper one case of the use of this drug is quoted in full, as it illustrates the difficulties and the problems of controlling spasms in the presence of decubitus ulcers. A summary of 20 other cases is provided. From these results one can conclude that this compound is extremely effective in controlling these particular spasms, without the production of undesirable side effects.

Pharmacology of Tigloidine.

Tigloidine is found as a minor alkaloid in the solanaceous plants *Duboisia myoporoides* and *D. leichhardtii*. The major alkaloids of these two plants are hyoscyamine (atropine) and hyoscyne. Chemically, tigloidine is a close homologue of atropine. Atropine is an ester of the aminoalcohol tropine with tropic acid; tigloidine is an ester of pseudo-tropine with tiglic acid, an alpha-beta unsaturated pentanoic acid (see Figure 1).

The parasympatholytic action of atropine and its homologues is to a large extent dependent on the presence of an alcoholic group and of a ring structure in the molecule of the esterifying acid. The esters of tropine or pseudo-tropine with saturated aliphatic acids show no clear-cut pharmacological action and are generally considered as being relatively non-toxic. Against parasympathicomimetic agents, like acetylcholine, carbamylcholine or methacholine, 50 to 60 mg. per kilogram of tigloidine showed only slight or no antagonistic effect under conditions in which 2 mg. per kilogram of atropine completely abolished the response of salivation, lachrymation or diarrhoea.

The LD₅₀ for small animals was of the order of 200 to 250 mg. per kilogram, the actual magnitude varying with the species and the strain. At near-lethal doses there were, at least in rats, some peripheral effects—namely, convulsive jerks—and it appeared that these high doses might potentiate the action of convulsant anaesthetics like "Cardiazol" or bemegride. At doses below 60 mg. per kilogram given intraperitoneally, no effect was noted on any of the animals tried (toads, mice, rats, guinea-pigs and dogs); the injected animals were indistinguishable from the controls. Prolonged medication of up to 150 mg. per kilogram given orally per day did not appear to have any effect on guinea-pigs after two to three weeks' medication.

When, however, tigloidine was tried on the sartorius preparation of the toad *Bufo marinus* (Trautner and MacCallum, 1949), it was found that it had in practically the same concentrations as atropine (1/2000 to 1/3000) exactly the same effect of quick fatigue after repetitive stimulation (at a rate of over five per second), an effect described by MacCallum (1949) as "delayed recovery". Furthermore, the effect was easily and completely reversible by removing the drug and allowing the muscle to recover in pure toad-Ringer medium.

On a basis of these observations, it was considered appropriate to try the drug as a substitute for atropine in disorders of central origin, when medication with atropine had proved helpful, but was limited by the early appearance of unpleasant side effects such as dryness in the throat, mydriasis or headache. Successful trials were made with a few cases of Parkinsonism (Trautner and Noack, 1951) and later with Huntington's chorea (Trautner and Gershon, 1958).

As was expected, no side effects of a parasympatholytic character were ever observed. Since in the toad experiments mentioned tigloidine had shown a depressant effect on the response of the sartorius to repetitive stimulation, it was feared that higher doses might cause in man depression or even paralysis of skeletal or other muscles. No such effect was ever observed, even if the daily doses were increased to 25-30 mg. per kilogram. With the doses used clinically, the drug appeared solely to depress overactive central integrating systems, and thus to reduce neuromuscular disturbances as manifested in Parkinsonism and Huntington's chorea, or after spinal injury. The only other effect noted was a tendency to produce an improvement in mood and general manageability.

Report of a Case.

Six years ago Mr. X, aged 27 years, became paraplegic after a traumatic fracture-dislocation of the tenth on the eleventh thoracic vertebra. Six months later he developed bilateral decubitus ulcers over both trochanters, with subsequent osteomyelitis and the onset of troublesome hip flexor spasms. Two years after his initial injury he was admitted to the Austin Hospital, Melbourne, for treatment. On April 24, 1954, he had a bilateral excision of the diseased tissues and bone. Despite some increased spasm, the left side healed and remained healed, but the right hip healed only temporarily. His spasms increased in severity, and on December 6, 1955, X-ray films showed multiple sequestra over the right trochanter. Whilst he was taking one gramme of mephenesin three times daily, the spasms became

after a week this was increased to 120 mg. six-hourly. Within ten days a profound change in the patient's condition occurred. The spasms were reduced in intensity, duration and frequency. The spasms seemed to spread into a ripply muscular contraction. After three weeks, the spasms were completely inhibited, and a two-stage plastic repair of the lesion was successfully undertaken. The post-operative phase proceeded smoothly, and there was union by first intention. For the first time in six years, and after six previous attempts, the right hip was free of infection. Eight weeks after the first successful control of spasm with tigloidine, a placebo was substituted. Within ten days the patient's spasms returned, although, now that the stimulus of the decubitus ulcer was absent, the rate and severity had decreased.

Within a month after tigloidine therapy was stopped, the patient developed cellulitis over his right buttock and his spasms became troublesome again. Resumption of tigloidine therapy abated the spasms and the infection was cleared. As the drug was in short supply, the therapy was ceased.

Three months later, the patient had an infected left ischial tuberosity bursa which again aggravated his spasms. One hundred and twenty milligrammes of tigloidine given thrice daily controlled the spasms, and plastic surgery to the area was successfully performed. After eight weeks the drug was again discontinued. The spasms of his hips did return, but were tolerable and did not interfere with his walking.

While on tigloidine therapy, the patient also showed a marked alteration in his attitude and social behaviour. Prior to the onset of treatment he was sullen, uncommunicative, irritable and given to outbursts of temper directed towards the nursing staff and his fellow patients. After the tigloidine therapy was established he became much more communicative, pleasant and cooperative. He also said that he felt brighter and more cheerful in himself. Even allowing for the fact that the patient felt something was being done to control his spasms, and hence that an improved outlook could be expected, the amount of mental improvement was most marked. This general effect on mood and general psychological sense of well-being were also observed in other patients.

Results.

The results are set out in Table I. The 21 patients in this series were all suffering from either post-traumatic paraplegia, or paraplegia due to tumour; all of them had muscular spasms of varying severity at the commencement of the trial. Some patients had spasms confined to muscle groups producing tremor, muscle fasciculation and jerking of the limbs, others had gross flexor spasm of the body producing acute flexion of the spine. The dosage employed in this series was up to 2000 mg. per day. On no occasion were side actions observed. One patient with gross spinal flexor spasm did not appear to be affected by the treatment. The other 20 patients were all favourably and very markedly influenced by the tigloidine medication. The muscle spasms, jerking and throwing about of limbs were greatly relieved in all cases. A double-blind test was used in this series on two separate occasions. The first placebo employed was lactose and starch, and the second was dextrose. In both of these trials with placebo the movements in all these patients became more frequent and more severe in intensity within seven days.

Discussion.

The cases presented demonstrate a beneficial effect of tigloidine, which is sometimes quite dramatic in cases in which spasticity, spasms or athetoid or choreiform movements are prominent symptoms. It is not claimed that the drug cures the conditions, and it must be emphasized that the observations show only an effect on the spasticity and on the intensity and frequency of the involuntary movements. The motor (muscular) disturbances in these patients were often severe enough to delay recovery or to affect the condition adversely, especially when they contributed to the formation of decubitus ulcers and similar complications, which are practically untreatable as long as the motor disturbance persists. It should be pointed out that control of spasms and spasticity by tigloidine allows of full voluntary movement, in contradistinction to the impairment of voluntary motor power seen with some

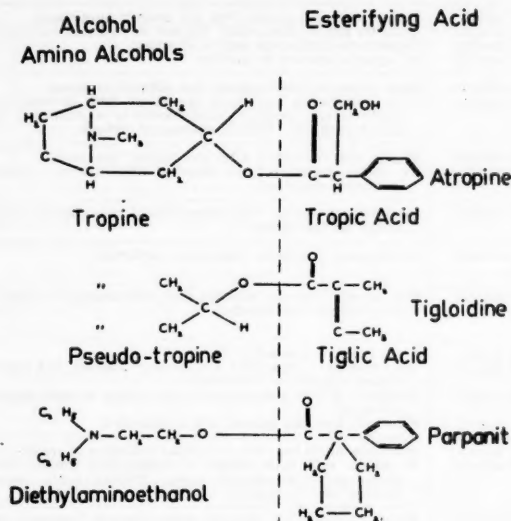


FIGURE I.

Formule of tigloidine and related compounds referred to in the text.

worse and the scar tissue broke down. Two months later, an attempted two-stage plastic flap rotation failed, presumably because of spasm (Snell, 1958), and four months later an anterior rhizotomy by crushing of first lumbar to the first sacral roots was performed. With abolition of spasms, another plastic repair was attempted, but unfortunately the area became secondarily infected and the spasms returned. The patient had now been in hospital for two years and was anxious to return home, so he was discharged.

On March 2, 1957, X was admitted to the newly created Spinal Unit of Victoria at the Austin Hospital for treatment of his chronically infected right trochanteric bursa. A sinogram showed a large pocket extending down the lateral aspect of the thigh. Three months of conservative treatment with daily irrigation and the local application of antibiotics failed to improve it. The spasms had decreased slightly, so a plastic procedure was performed on May 14, 1957. Despite excision of the infected bone and tissue, the flexor spasms became uncontrollable, and by the fifth post-operative day the sutures had cut out, leaving a large defect. The wound was resutured and the patient sedated with five grains of phenobarbitone daily, to which was added 1.5 grammes of mephenesin daily. This had no effect on the spasms. Eight weeks after the operation *débridement* was carried out and the wound was resutured, but without success. Further operative procedures were suspended until such time as the spasms were controlled. Phenobarbitone was discontinued and propantheline bromide 200 mg. three times a day and 300 mg. *nocte* given instead. Methanelline bromide in large doses was said to have a curare-like action (Krantz and Carr, 1958). After 24 hours severe dryness of the mouth and diplopia resulted, and the drug was ceased.

On August 17, 1957, the patient was started on a clinical trial of tigloidine in a dosage of 40 mg. six-hourly, and

TABLE I.
Tigloidine in Paraplegic Spasticity.

Case Number.	Age. (Years.)	Condition at Outset.	Dose. (Milligrammes per Day.)	Duration.	Response.
1	38	Incomplete quadriplegia sixth cervical level. Marked spasm of legs.	640 Discontinued 980	3 months. 1 month. 3 months.	Spasms diminished considerably. Recurrence of spasm, within a week of cessation. Reduction in spasms again, up in a chair.
2	35	Complete paraplegia, sixth thoracic level.	640 Discontinued 800	1 month. 2 months. 2 months.	Spasms considerably and almost completely abolished. Previous trial with mephenesin ineffective. Recurrence of spasms. Gross extensor spasms present and also urinary retention. Spasms again relieved, general spasticity less. Complete freedom from spasm at night.
3	36	Complete paraplegia, sixth thoracic level.	320 640 Discontinued 960	1 month. 1 month. 2 months. 2 months.	Spasms were less severe, but not entirely suppressed. Adductor spasms diminished. Urinary incontinence relieved. Recurrence of previous degree of spasm. All spasms lessened in severity.
4	21	Spastic cerebral palsy. Dysarthria, spasticity of all limbs and some choreiform movement of them.	480 960	2 months. 3 months.	Some apparent improvement, but difficult to assess. Some lessening of choreiform movement, with decrease in spasticity and resultant improvement in coordination of limb movement. Overall assessment difficult.
5	41	Paraplegia, sixth thoracic level. Spasms and spasticity of the legs.	240 960	2 months. 2 months.	Spasms well controlled after two weeks' treatment. As above—transferred to Rehabilitation Centre, where treatment continued.
6	32	Paraplegia, sixth thoracic level. Spasms and spasticity of legs.	640	1 month.	Inhibition of spasms, with improvement in continence and ability to pass urine.
7	46	Spinal cord tumour. Severe degree of spasms.	640	1 month.	No response. Anterior rhizotomy performed.
8	40	Paraplegia. Plastic graft done for decubitus ulcer. Spasms very severe and mephenesin tried without effect.	640	2 months.	Good result. Spasms inhibited and good healing of wound. Feels bright and cheerful.
9	47	Paraplegia, twelfth thoracic level. Spasticity of legs with spasms, most marked at night.	320 960 Discontinued 960	2 weeks. 2 months. 2 months. 1 month.	Some relief of spasticity. Good response. Spasticity considerably lessened, and night spasms completely controlled. Spasticity of very severe degree, and spasms at night again prevalent. Spasticity less and spasms again controlled.
10	55	Quadriplegia, sixth cervical level. Severe spasticity of all four limbs with spasms.	640 960	1 month. 3 months.	Spasticity much less, but only slight inhibition of spasms. As above, with more control of spasms and considerable improvement in mental state. Patient much more cheerful and cooperative.
11	32	Quadriplegia, seventh cervical level. Severe spasms.	1000	2 months.	Some inhibition of spasms, with marked lessening of spasticity.
12	16	Quadriplegia—fracture of the third and fourth cervical vertebrae. Gross spasms with mass reflex reaction from stimulus. Spasms with marked rigidity in both arms. Violent body movements causing throwing about in bed.	640 1000 Discontinued	1 month. 2 months.	Patient showed a good response. Spasms lessened in frequency, and spasticity considerably lessened. Violent body movements controlled, spasticity and spasms lessened. Recurrence of all symptoms; spasms and spasticity as before treatment—irradiation response returned.
13	42	Incomplete quadriplegia, with spasticity of lower limbs causing considerable difficulty in walking.	800	1 month.	Walking improved; spasm and spasticity less; less spasm at night.
14	20	Brown-Séquard syndrome, fifth thoracic level. Severe spasm and clonus in left leg.	1000	2 months.	Good response; severity of spasms decreased. Clonus lasts much shorter period. Able to get up and about, and left leg does not interfere with walking.
15	23	Post-traumatic left hemiplegia, with aphasia and rhinophonia.	1000	2 months.	Diminution in spasms and spasticity, with resultant improvement in coordination. Better articulation and generally more cooperative.
16	62	Spinal cord tumour. Paraplegia in flexion with marked adductor spasms of legs.	320	2 weeks. 6 weeks.	Improvement on initial dose, but more marked on increased dosage. Adductor spasms almost completely relieved.
17	58	Spinal cord tumour. Incomplete paraplegia with spasms of both legs.	320 640	2 weeks. 6 weeks.	Marked decrease in severity of spasms. Almost complete control. Treatment continued to be effective after laminectomy, as tumour not removed.
18	23	Transverse myelitis. Severe flexor and extensor spasms and adductor spasms inhibiting voluntary action.	900	1 month.	Spasms much improved and regaining voluntary movement.
19	26	Head injury, mid-brain damage. Spasms of hamstrings interfering with walking.	400	1 month.	Spasm of hamstrings now controlled and walking well.
20	44	Ependymoma of cord. Laminectomy with attempts at removal six months prior to present trial. Gross flexion spasms with some voluntary motor power.	600	6 weeks.	Spasms have been controlled, and voluntary power is now more effective.

other lissive agents. Especially it was shown to be of benefit in controlling spasms so that skin grafting could be undertaken with a more favourable outcome.

It should be stressed that the assessment of change in these patients is difficult, as no objective measures are

available. In the final analysis observation and careful clinical assessment by several independent observers are the only estimates that can be applied; but a double-blind control was carried out on every patient on at least one occasion. As a result of this study it may be stated that

the use of tigloidine did produce significant improvement in the patients. Moreover, in many of the patients an improvement in mental state was also observed, and this is to be further investigated in psychiatric states.

Initial experience with the use of tigloidine in children with cerebral palsy of both the spastic and athetoid types indicates that varying degrees of control may be obtained. It should be noted that if, owing to the efforts of the patient to compensate the disturbance caused by a given spastic muscle group, there is an imbalance between agonists and antagonists, this imbalance will not be affected by the drug. Its correction will be attained by physiotherapy and training. Therefore there may be, in these patients especially, an initial deterioration in function. The spasms may be controlled by the drug, but the patient is not capable of regulating and controlling the impulses now going to the spasm-free muscles and their antagonists.

The present study does not give much specific information as to the mechanism and site of action of tigloidine. It seems, however, very unlikely that the main point of attack of the drug is in the periphery of the neuromuscular system. A central site of action involving the motor-integrating systems seems more likely. This central site of action is also indicated by the effect on behaviour generally, and by the mild euphoria often observed in these patients.

In conclusion, it may be said that the therapeutic effects found in the various types of neuromuscular disorders examined to date justify further clinical trials.

Summary.

Tigloidine hydrobromide was tried in 21 cases of paraplegia with spasm and spasticity. Marked relief of both symptoms has been produced in these patients. The efficacy of the medication has been confirmed by the use of double-blind controls.

The control of spasms and spasticity has made the patients generally more comfortable and their sleep less disturbed, and mood and manageability have been improved. Furthermore, the use of tigloidine has enabled plastic repair to be undertaken with success.

Chemically, tigloidine is a homologue of atropine, but it shows neither in animals nor in man any marked parasympatholytic action, nor does it to any significant degree counteract parasympathomimetic drugs like carbamylcholine.

Experiments with fairly high concentrations on the isolated sartorius of the toad showed a quick fatigue of the muscle on repetitive stimulation, but experiments with guinea-pigs given subtoxic doses (100 to 150 mg. per kilogram per day) for three weeks failed to show any effect on skeletal muscle. The animals showed neither sluggishness nor drowsiness, and in fact were indistinguishable from the controls. Toxic doses of the drug in mice (250 mg. per kilogram) caused convulsions and death, and it was found in small animals that the effect of subconvulsive doses of other central excitants as bemegride may be potentiated by high doses of tigloidine (100 mg. per kilogram).

A range of dosage in man up to about 30 mg. per kilogram has produced no toxic or side effects, even on prolonged medication up to 12 months.

Results to date justify further clinical trials.

Acknowledgements.

We wish to thank Dr. D. G. Duffy and Mr. K. C. Bradley, of the honorary medical staff at the Austin Hospital, for permission to publish the case material, and also the Medical Superintendent, Dr. W. Moon, for his unfailing attention to our needs. Funds for this investigation were donated by Glaxo Laboratories (Aust.) Pty. Ltd., who also supplied the tigloidine. Technical assistance was provided by the Medical Research Funds and Mental Health Fund of the University of Melbourne.

Bibliography.

- BAKER, A. B. (1955), "Spinal Cord Trauma", in "Clinical Neurology", New York, 14: 1424.
- BASMAJIAN, J. V., and SZATMARI, A. (1955), "Chlorpromazine and Human Spasticity", *Neurology*, 5: 856.
- BERGER, F. M., and BRADLEY, W. (1946), "The Pharmacological Properties of Dihydroxy-(2-Methylphenoxy)-Propane (Myanesin)", *Brit. J. Pharmacol.*, 1: 265.
- GOODMAN, L. S., and GILMAN, A. (1941), "The Pharmacological Basis of Therapeutics", 2nd Edition, Macmillan, New York, 131.
- GUTTMANN, L. (1957), "The Treatment of Spasm in Spinal Injuries", *Bull. post-grad. Comm. Med. Uni. Sydney*, 13: 47.
- HENNEMAN, E., KAPLAN, A., and UNNA, K. (1949), "Neuropharmacological Study on the Effect of Myanesin (Tolserol) on Motor Systems", *J. Pharmacol. exp. Ther.*, 97: 331.
- KUHN, R. A., and BICKERS, D. S. (1948), "An Evaluation of Curare in Spasticity due to Spinal Cord Injuries", *New Engl. J. Med.*, 238: 615.
- KRANTZ, J. C., and CARR, J. C. (1958), "Central Nervous System Depressants: Hyperkinesia, Epilepsy, Paralysis Agitans and Chorea", in "Pharmacological Principles of Medical Practice", 4th Edition, Williams & Wilkins, Baltimore, 617.
- MACCALLUM, M., MACCALLUM, I. A. N., and SHAW, F. M. (1949), "The Action of Yohimbine on Excitation and Prognation in Nerve", *Aust. J. exp. Biol. med. Sci.*, 27: 115.
- MAJOUR, H. W., and RHINE, R. (1947), personal communication.
- MUNRO, D. (1952), "The Treatment of Injuries of the Nervous System", Saunders, Philadelphia, 155.
- MUNRO, D. (1952), "Case Records of the Massachusetts General Hospital", "Diseases of the Thyroid Gland", *New Engl. J. Med.*, 233, 453.
- SNELL, J. A. (1953), "Two Stage Plastic Flap Operation", *Med. J. Aust.*, 2: 109.
- TRAUTNER, E. M., and GERSHON, S. (1953), "The Effect of Tigloidine on Extrapyramidal Syndromes (Huntington's Chorea)", *Aust. Ann. Med.*, 7: 286.
- TRAUTNER, E. M., and MACCALLUM, I. A. N. (1950), "The Action of Tropine and Heliotridine Alkaloids on Excitation, Propagation and Recovery in Muscle", *Aust. J. exp. Biol. med. Sci.*, 28: 343.
- TRAUTNER, E. M., and NOACK, C. M. (1951), "Tigloidine as a Substitute for Atropine in the Treatment of Parkinsonism", *Med. J. Aust.*, 1: 751.
- WISLICKI, L. (1953), "The Influence of Chlorpromazine on Neuromuscular Transmission and on the Action of Muscle Relaxants", *Arch. int. Pharmacodyn.*, 115: 52.

CHLOROTHIAZIDE IN RENAL DISEASE.¹

By H. M. WHYTE,

Clinical Research Department, Kanematsu Institute, Sydney Hospital.

THE principal uses of chlorothiazide are as a diuretic agent in the treatment of oedema and as an adjuvant in the treatment of hypertension. But the final common pathway for its actions, whether they are desirable or undesirable, is the kidney, for it is by altering the pattern of renal function that chlorothiazide acts. It is obviously important, therefore, that we should consider whether the action of chlorothiazide is in any way altered when the kidneys are diseased; whether its therapeutic efficacy is impaired; whether it causes ill-effects; whether, indeed, it works at all. I am not here concerned with enumerating in detail all the experiences, personal and published, of chlorothiazide in renal disease, but rather with stating the general principles and points of practical management that have emerged.

Two slightly different, though related, aspects of this problem should be kept in mind. The first concerns the use of chlorothiazide in treating manifestations of primary renal disease when renal dysfunction is recognized as being present and as causing the features for which treatment is being given. The second concerns the use of chlorothiazide in treating hypertension, or oedema, not primarily of renal origin, but with which renal disease is coincidentally present, perhaps unrecognized, and may be affecting the action and efficacy of the drug.

¹Read at the International Symposium on Chlorothiazide and Other Diuretics at the University of Hong Kong in November, 1958.

Oedema and Hypertension in Renal Disease.

Both oedema and hypertension are frequently associated with renal disease. Hypertension occurs clearly associated with renal disorder in acute nephritis, in chronic renal insufficiency (usually chronic glomerulonephritis or chronic pyelonephritis), and in a variety of rarer conditions, such as congenital malformations and lesions of the renal arteries. These diseases affect renal function in different ways, so that, even though they have one feature in common—namely hypertension—they differ in other respects, which may well include their responsiveness to a drug like chlorothiazide.

Nephrotic Oedema.

The aim in using chlorothiazide in nephrosis is to reduce oedema, and this is successfully achieved in the majority of cases. A typical result is shown in Figure I, with

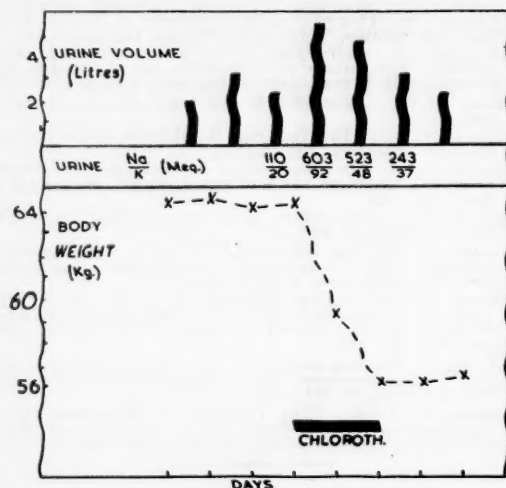


FIGURE I.

Diuresis induced by chlorothiazide in a patient with nephrotic oedema.

diuresis, an increase in the urinary loss of sodium and to some extent potassium, and a loss of 8 kg. in weight with disappearance of oedema. This is a common response, reported by many observers, in various forms of the nephrotic syndrome: "pure nephrosis", subacute glomerulonephritis, the Kimmelstiel-Wilson complication of diabetes, lupus nephritis and amyloid disease. Of course, the disease process itself is unaffected, and proteinuria continues; but chlorothiazide very effectively removes one of the most troublesome features of the disease by causing the kidneys to lose salt and water.

Sometimes chlorothiazide has been found to induce diuresis when other treatments have failed. For example, Slater and Nabarro (1958) had one patient whose oedema persisted despite treatment with a diet of low sodium content, prednisone and mersalyl injections; but prompt diuresis occurred when chlorothiazide was given. In other cases, chlorothiazide has been effective only when combined with other forms of treatment. Schreiner (1958) describes experiences of this sort. One of his patients was a child who failed to respond to steroids, albumin infusions, chlorothiazide or a mercurial diuretic when each was given alone; but diuresis occurred when chlorothiazide was combined with ACTH and intravenous infusions of albumin. In other instances diuresis may be successfully induced by steroid therapy, or albumin or some other form of treatment, or may even occur spontaneously, but chlorothiazide naturally enhances the effect.

It is often impossible to know exactly what has initiated diuresis.

In Figure II is shown the resolution of oedema and, in fact, the complete remission of a nephrotic episode in a boy aged six years. This attack, which was a relapse occurring one year after the first episode, was not a severe one, but there was slight generalized oedema, and the serum albumin content was only 1.5 grammes per 100 ml. Within three or four days of starting the combined treatment of prednisolone and chlorothiazide, the sodium excretion increased and diuresis occurred, with disappearance of protein from the urine.

Regardless of whether success was due to one or other or both drugs, there is something to be said in favour of giving chlorothiazide with the steroids, in that it may offset any tendency towards increased sodium retention. This should also apply in the post-diuretic period when treatment with steroids is being continued. It is worth remembering that the potassium loss induced by steroids is increased by chlorothiazide, so that it becomes imperative to ensure an adequate intake of potassium either in food or in tablet form.

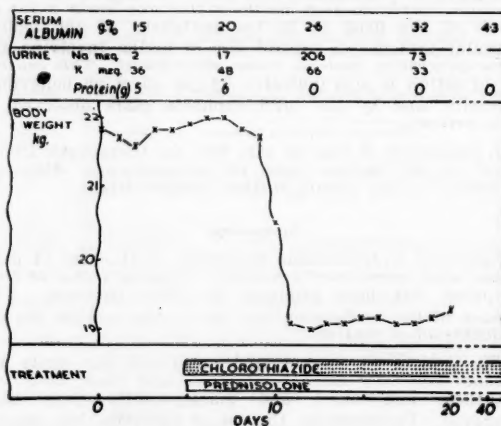


FIGURE II.

Diuresis and remission of nephrosis following treatment with prednisolone and chlorothiazide in a child with relapsing diffuse membranous glomerulonephritis.

Even after diuresis has occurred and oedema has disappeared, it is often useful to continue treatment with chlorothiazide. Not only does it counteract any tendency for steroids to cause salt retention, but even when steroids are not being given it should help to prevent the reaccumulation of salt and water, and allow of the addition of salt to an otherwise unpalatable diet. For this purpose the body weight can be used as a guide to hydration, and chlorothiazide taken whenever the weight rises by four pounds or so.

Thus chlorothiazide, taken by itself, may be successful in causing the resolution of nephrotic oedema, even after other treatments have failed; or it may be successful only when combined with other forms of treatment; or it may enhance the diuresis already induced in other ways; or it may prevent the situation from being made worse by steroids.

Sometimes, however, chlorothiazide, like other therapeutic agents, fails to relieve nephrotic oedema, just as it occasionally fails to relieve ascites in hepatic cirrhosis or oedema in cardiac failure. Schreiner mentions several instances. The course of another is illustrated in Figure III.

This man had a relapse of nephrosis of undetermined cause and was grossly oedematous, with a serum albumin level of about 1 gramme per 100 ml., a serum cholesterol content of over 1000 mg. per 100 ml., heavy proteinuria, a normal glomerular filtration rate, normal serum electrolyte levels and no sodium in his urine. No response was obtained to a salt-free diet, a mercurial diuretic, ion-

exchange resin, chlorothiazide, a carbonic anhydrase inhibitor, or repeated large infusions of albumin. However, two weeks after the start of treatment with cortisone, diuresis started. This appeared to coincide with the giving of nitrogen mustard, but analysis of the urine showed that sodium excretion had begun earlier. Diuresis was massive, and the patient lost some 20 kg.—three stone—in weight within a few days. Subsequently his urine became protein-free and the level of albumin in the serum rose to normal.

exchange mechanisms are important. Chlorothiazide primarily inhibits the reabsorption of sodium, and it may conceivably fail to work significantly for a number of reasons (Table I). Inadequate dosage is one. It must be remembered that chlorothiazide is distributed through the extracellular water, and, as this may be increased twofold or threefold in nephrotics, the dose may have to be two or three times as great as normally employed to achieve the same concentration. A dosage of four grammes

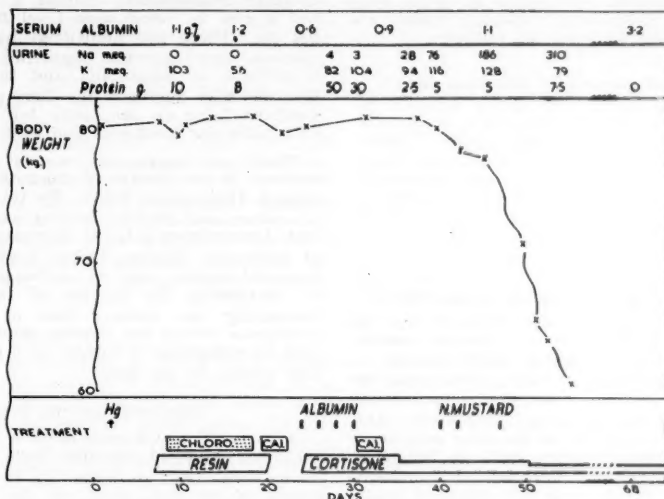


FIGURE III.

The clinical course of a patient with massive nephrotic edema failing to respond to chlorothiazide and other forms of treatment.

Why should chlorothiazide sometimes fail to cause diuresis? Recall for a moment how chlorothiazide normally exerts its action. The renal excretion of sodium depends on an adequate renal blood supply, the production of a

per day is commonly required. If the glomerular filtration rate is very low, then chlorothiazide is often ineffective; that is when too little sodium is presented to the tubules. Schreiner makes this point very strongly, and it explains why the drug is better in "pure" nephrosis than for nephrotics with azotemia. It also explains why it sometimes works only when combined with other forms of treatment, such as steroids or infusions of albumin, which cause some increase in glomerular filtration. It must be

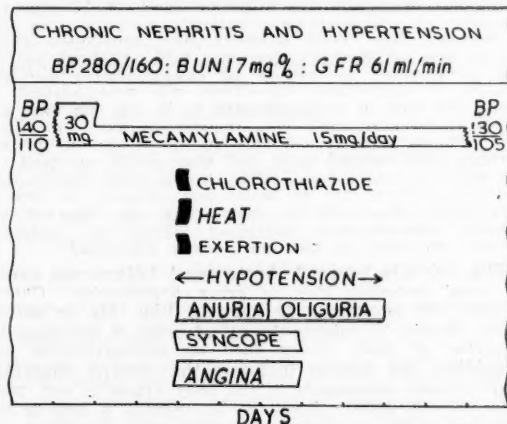


FIGURE IV.

The precipitation of severe hypotension and consequent troubles by chlorothiazide and other factors in a patient with chronic nephritis under treatment with ganglion-blocking drugs for hypertension.

sufficient volume of glomerular filtrate and then judicious reabsorption by the tubules. Thus blood flow, glomerular filtration rate and factors like aldosterone and the ion-

TABLE I.

Possible Causes of Failure of Response to Chlorothiazide and Suggested Methods of Dealing with the Situation.

Cause of Failure.	Treatment.
Dose inadequate.	Increase dose—up to eight grammes daily.
Glomerular filtration too low.	Increase glomerular filtration rate—steroids, albumin, "Dextran", Expand plasma—albumin, "Dextran".
Tubular reabsorption of sodium too avid (e.g., aldosteronism).	Give other diuretics—mercurial, carbonic anhydrase inhibitor.

borne in mind, too, that excessive diuresis caused by chlorothiazide or any other means may result in an excessive loss of sodium, a shrinkage of blood volume and some impairment of the glomerular filtration rate. This may perhaps account for the development of refractoriness to the drug, as reported in two nephrotic children by Laragh (1958).

Another reason for the failure of chlorothiazide to inhibit the reabsorption of sodium may be the presence of excessively strong reabsorptive influences, such, for instance, as the presence of aldosterone in excess. This can be presumed to be the case in patients with severe

nephrosis, whose serum protein level is very low, as in the case illustrated earlier, and in advanced hepatic cirrhosis. Chlorothiazide does not antagonize aldosterone (Beyer, 1958). The competition may possibly be overcome by expanding the plasma volume with albumin or dextran, thereby reducing the stimulus for production of aldosterone. Finally, failure may give way to success if the action of chlorothiazide is reinforced by other diuretics, such as mercurial ones or carbonic anhydrase inhibitors.

What dangers or ill-effects are likely to arise from using chlorothiazide in nephrosis? Usually there are none, but rarely there may be some, as follows:

With diuresis:

Further reduction of glomerular filtration rate

Increased azotemia

Low-salt state

Refractoriness

Hypotension

Hypokalemia

Digitalis intoxication

Without diuresis:

Excessive loss of potassium

(Watch serum levels and give potassium supplements.)

If diuresis occurs in a patient who already has an abnormally low glomerular filtration rate, further impairment of filtration may occur (Bradley, 1958) leading to increased azotemia. Occasionally the loss of salt may be so great as to induce a low-salt state. Refractoriness to the drug may develop, as was mentioned previously. And, of course, the more common effects of the drug may occur—namely, lowering of blood pressure, even to the point of hypotension with symptoms, a lowering of the serum potassium level (though rarely does this produce symptoms) and digitalis intoxication. The serum potassium level fell as low as 1.8 mEq/l. in one reported case (Schreiner, 1958). Even if diuresis does not occur, potassium may be lost to excess in the urine. Laragh emphasizes the point that chlorothiazide causes relatively greater loss of potassium than sodium in conditions such as sodium depletion, in which sodium reabsorption is being very powerfully promoted, presumably by aldosterone. Obviously, serum levels of urea, sodium and potassium must be checked from time to time, and potassium supplements given by mouth either as a routine, or at least when the serum level falls below normal. In spite of the fact that high dosage is sometimes used, and renal excretion of the drug is often subnormal, no untoward toxic effects have been reported other than an occasional rash and alimentary upset, and in two cases glycosuria has been found (Slater and Nabarro, 1958). Warnings have been given that the hypokalemia caused by chlorothiazide may cause superadded damage to the kidneys, but this seems unlikely.

Other Renal Diseases.

Let us consider briefly the place of chlorothiazide in the treatment of other renal disease.

It is rarely called for in acute glomerulonephritis. However, fluid retention is the rule in this disease, and chlorothiazide may prove useful when there is severe oedema, hypertension, pulmonary oedema or encephalopathy. It is stated to be efficacious (Schreiner, 1958), but in view of the impaired glomerular filtration it would not be surprising if it did not always work. However, a group of hospitals in Sydney is cooperating in testing its efficacy in a strictly controlled trial on patients with uncomplicated acute nephritis. This is being combined with a trial of prednisolone. There are good reasons why steroid therapy may be helpful, and some workers hold that it is (Danowski and Mateer, 1957). One of the main drawbacks to the use of steroids has been the fear of salt retention, and this may be offset by the action of chlorothiazide. It is as yet too soon for our trial to yield any conclusions.

Oedema in chronic renal insufficiency is usually of cardiac origin, due to hypertensive or ischaemic heart

disease, and the aid of a diuretic may be sought. Chlorothiazide is usually effective, but it may fail to act because of a low glomerular filtration rate or, having promoted diuresis, it may further impair the glomerular filtration rate and make uraemia worse. Watson *et alii* (1958) described the production of substantial diuresis in one patient, but the blood urea level rose from 146 to 236 mg. per 100 ml. Bayliss *et alii* (1958) had a patient with hypertension and chronic renal insufficiency who became almost free of oedema spontaneously, and in whom chlorothiazide subsequently caused a further loss of weight and a rise in blood urea level from 50 to 150 mg. per 100 ml. There are additional hazards in chronic renal disease. Some chronic nephritics lose excessive amounts of sodium or potassium, and in these patients chlorothiazide may increase the loss and produce a "low-salt syndrome", or an unusually low serum potassium level, with muscular weakness and even paresis.

There are, moreover, two or three additional points claimed to the credit of chlorothiazide in chronic renal disease (Schreiner, 1958). By inhibiting the reabsorption of sodium and thereby causing osmotic diuresis, it is said that it sometimes helps to decrease uraemia. In some cases of polycystic disease, it has been found to decrease the hyperchloraemia, and to decrease abdominal discomfort by decreasing the tension of the cysts. Moreover, by increasing the urinary loss of sodium, chlorothiazide sometimes allows the chronic nephritic, who would otherwise be compelled to subsist on a salt-free diet, to add salt and savour to his food.

Hypertension and Renal Diseases.

Hypertension and renal disease are frequently associated. Although chlorothiazide may have some hypotensive action in its own right, its main use is as an adjuvant to other forms of therapy, such as the administration of the ganglion-blocking agents. Even in ordinary circumstances this is sometimes a powerful combination, but in the presence of renal disease it may be so potent as to be dangerous or even disastrous. Figure IV is an example of this.

This illustrates the main points in the recent history of a woman patient aged 48 years, who had suffered from nephrotic oedema for one year at the age of 27 years, and then reported to our hospital several months ago with evidence of chronic renal insufficiency and severe hypertension uncontrolled by pentolinium. She had "heavy" proteinuria, a blood urea nitrogen level of 17 mg. per 100 ml., and a glomerular filtration rate which was 50% of normal. Her blood pressure was constantly about 280/160 mm. of mercury, but was held at about 140/100 mm. of mercury by 30 mg. of mecamylamine per day. Because of intolerable side-effects she was advised to reduce the dose of mecamylamine to 15 mg. per day, and two days later to take chlorothiazide as well. She took chlorothiazide, and worked hard in her house on one hot morning. She became faint, and was unable to stand up, she had repeated attacks of angina pectoris, she became completely anuric for 48 hours and oliguric for several days more. She took no more than one dose of the diuretic, unfortunately continued taking the ganglion-blocker, remained in bed and luckily recovered.

Why did this happen? Acute renal failure was caused by renal ischaemia due to gross hypotension. Chlorothiazide can contribute to episodes like this in several ways. Firstly, by raising the pH of urine, it decreases the excretion of basic drugs such as mecamylamine and pempidine, and thereby increases the effective concentration of these compounds in the body (Baer *et alii*, 1956; Milne *et alii*, 1958). Secondly, by causing a loss of salt and water, it reduces the plasma volume and thereby increases the hypotensive response to ganglion blockade. Thirdly, as a consequence of salt loss, shrinkage of plasma and lowering of blood pressure, there will be a decrease in the glomerular filtration rate, which will cause further retention of the ganglion-blocking drug. A vicious circle is set up, which is made worse, of course, if the patient keeps on taking the treatment.

These ill-effects are not peculiar to chlorothiazide, but are likely to occur when any diuretic is used. They are

especially likely to occur if the patient is already salt-deficient as a result of taking a salt-poor diet, of previous treatment with diuretics or of a salt-losing form of nephritis. When the production of urine falls, chlorothiazide is retained within the body, except for what is excreted in the bile, but luckily it is a non-toxic substance (Beyer, 1958).

What, then, should be the plan of action when chlorothiazide is to be used to treat hypertension in patients with renal disease? The state of the serum sodium and potassium levels should be checked. There should be a normal, but not over-liberal, amount of salt in the diet, unless this is absolutely intolerable, and the true state of the blood pressure should be known from serial recordings. Most patients will already be under treatment with some hypotensive agent such as mecamlamine. This should be reduced to half dosage for at least two days before chlorothiazide is given under supervision, and the effect of the combined therapy should be assessed by taking frequent measurements of the blood pressure. Dosages must then be adjusted, and it must be remembered that these patients may be more than ordinarily prone to develop hypotension with overheating, exercise or infection. Renal infection is particularly likely to cause trouble.

Conclusion.

In conclusion, let me pick out some of the main points regarding the use of chlorothiazide in renal disease. It is useful in treating oedema and hypertension, and as a diuretic it has some advantages over other types. Unlike mercurial preparations, it is free from the suspicion that it causes any renal damage. And unlike the carbonic anhydrase inhibitors, it can work in the presence of acidosis, which, of course, is common in renal disease, and it does not cause acidosis. It is usually effective, but this depends upon the presence of an adequate glomerular filtration rate and the absence of excessively avid tubular reabsorption of sodium. Apart from the ordinary side effects which may occur, such as hypokalaemia and digitalis intoxication, it may cause further impairment of renal function with a drop in the glomerular filtration rate, increased azotemia and perhaps accentuated salt loss in a salt-losing type of nephritis. Marked hypotension may occur if the ganglion-blocking drugs are being given concurrently. In the final stages of renal disease, of course, we can expect no effective response to chlorothiazide or to any other drug which relies for its effectiveness on a functional response from the organ which is diseased.

References.

- BAER, J. E., PAULSON, S. F., RUSSO, H. F., and BEYER, K. H. (1956), "Renal Elimination of 3-Methylaminoisocamphane Hydrochloride (Mecamlamine)", *Amer. J. Physiol.*, 186: 180.
- BAYLISS, R. I. S., MARRACK, D., PIRKIS, J., REES, J. R., and ZILVA, J. F. (1958), "Chlorothiazide: An Oral Diuretic", *Lancet*, 1: 120.
- BEYER, K. H. (1958), "The Mechanism of Action of 'Chlorothiazide'", *Ann. N.Y. Acad. Sci.*, 71: 363.
- BRADLEY, S. E. (1958), "Difficulties in the Appraisal of Disturbances in Fluid and Electrolyte Metabolism in Clinical Medicine", *Ann. N.Y. Acad. Sci.*, 71: 391.
- DANOWSKI, T. S., and MATHER, F. M. (1957), "Therapy of Acute and Chronic Glomerulonephritis", *J. chron. Dis.*, 5: 122.
- LARAGH, J. H. (1958), "Some Effects of Chlorothiazide on Electrolyte Metabolism and its Use in Edematous States", *Ann. N.Y. Acad. Sci.*, 71: 409.
- MILNE, M. D., SCHREINER, B. H., and CRAWFORD, M. A. (1958), "Non-ionic Diffusion and the Excretion of Weak Acids and Bases", *Amer. J. Med.*, 24: 709.
- SCHREINER, G. E. (1958), "Chlorothiazide in Renal Disease", *Ann. N.Y. Acad. Sci.*, 71: 420.
- SLATER, J. D. G., and NABARRO, J. D. N. (1958), "Clinical Experience with Chlorothiazide", *Lancet*, 1: 124.
- WATSON, W. C., THOMPSON, T. J., and BUCHANAN, J. M. (1958), "Clinical and Laboratory Studies with Chlorothiazide: An Oral Diuretic", *Lancet*, 1: 1199.

AN OUTBREAK OF BACILLARY DYSENTERY.

By G. A. RICKARBY,

Acting Medical Officer of Health, Mansfield,

G. N. COOPER AND T. McAVAN,

Public Health Laboratory, University of Melbourne,

AND

J. E. COCKERILL,

District Health Officer, Public Health Department,
Melbourne.

AFTER a survey of the incidence of *Shigella* infections in Victoria during the period 1952-1957, it was suggested that these were gradually declining in this State (Cooper, 1958). While this may still generally be true, particularly in Melbourne, the present report underlines the fact that such infections may occasionally reach epidemic proportions. In the previous communication certain significant epidemiological features of shigellosis were discussed; the facts elicited during the investigation of the present outbreak entirely support the views expressed previously. In addition, the outbreak reported here serves as an excellent illustration of the many problems associated with the control and prevention of such epidemics in the general community.

The outbreak, attributed to *Shigella sonnei*, occurred in Mansfield, a town of some 2000 people situated in the north-east of Victoria. While essentially it serves as a central township for the surrounding farming community, its main industry is timber-milling, there being 13 mills situated on the outskirts of the township. Housing communities, both at the mills and in the town, have been provided by the mills for the lumber-workers. In general these houses are of poor quality and are unsewered; in some instances the night-pan service is not used and the disposal systems are quite primitive. Such conditions, of course, were entirely favourable for the initiation and subsequent dissemination of the infection throughout the community.

History of the Epidemic.

In February, 1958, three cases of infantile gastroenteritis were notified by one of us (G.A.R.) to the State Public Health Department. All three babies responded rapidly to phthalylsulphathiazole therapy; bacteriological examinations were not carried out at the time and, while some connexion is thought probable, there was no evidence to link these directly with the major outbreak. During the next six weeks no intestinal infections were reported to either of the two medical practitioners in the town.

On April 9, 10 and 11 a total of four infants were seen; all were passing blood and mucus in their stools, but otherwise were not clinically ill. All children again responded rapidly to sulphonamide therapy. Three of these patients lived in one of the timber-mill housing communities, the other coming from an outlying farm. On April 12, a patient was admitted to Mansfield District Hospital in a state of collapse, with a history of severe vomiting and diarrhoea for the past 12 hours (see Case 1). This patient had been in contact with one of the children seen several days earlier. Later (April 15), four young children were admitted to hospital with severe vomiting and diarrhoea; two of these children lived in the "mill town", while the remaining two lived in the mill's housing community situated in Mansfield itself. Bacteriological examination of faeces from the patients was sought, and the Public Health Laboratory reported the isolation of *Sh. sonnei* in all four cases.

During the following week an increasing number of cases were reported, mainly in school-age children and their younger siblings; later, many adult patients were seen, and within the course of two weeks the outbreak had assumed epidemic proportions. The epidemic continued throughout the month of May, and finally terminated in the first week of June. In the period from

April 9 to May 31, 188 cases of bacillary dysentery were reported to the State Health Department. In addition to these reported cases, when the known patients and their contacts were questioned, a further 133 people were found to have had diarrhoea and/or vomiting episodes which in their opinion did not warrant medical attention. Thus a total of 321 cases were known to have occurred during the outbreak; apart from these, many more townspeople had probably been infected, but had failed to report their "vague stomach upsets or slight diarrhoea". The outbreak was not confined to the town of Mansfield, for cases were reported throughout the outlying farm communities. There was extremely good evidence for believing that these patients were infected as a result of direct personal contact with the people of Mansfield.

Table I records the week-by-week incidence of infection in adults, school children and pre-school-age children during the eight weeks of the epidemic. The figures included in this table record only those patients who were seen by one of the local medical practitioners and reported to the State Health Department, or from whom *Sh. sonnei* was isolated on examination of faeces or rectal swabs. It is evident that, while initially the majority of

TABLE I.
Weekly Incidence of *Shigella Sonnei* Infection.

Age Group.	1958: Number of Cases Reported, Week Ending								Total Cases Reported.
	15/4	22/4	29/4	5/5	12/5	19/5	26/5	2/6	
Adult	1	1	13	16	21	25	4	0	81
School age ..	2	3	5	11	9	10	2	1	43
Pre-school age	6	6	4	9	8	22	7	2	64
Total	9	10	22	36	38	57	13	3	188

infections arose in children, the infection during the height of the epidemic was more commonly seen in adults than in the lower age groups. As the epidemic waned, however, the infection apparently persisted longer in the younger children. The apparent concentration of infection in adults and pre-school-age children is supported by the figures recorded in Table II, in which the incidence in these three age groups is compared; these figures include both notified cases and those subjects who had stated, on being interviewed, that they had had considerable vomiting and diarrhoea during the outbreak. As will be seen later, this may have been due to the surprising variation of symptoms observed in these various age groups.

Bacteriological Investigations.

After the isolation of *Sh. sonnei* in four of the early cases (*vide supra*) and the rapid development of the epidemic, an emergency laboratory was established by the Public Health Laboratory at the Mansfield District Hospital. This laboratory was equipped in such a way as to allow the rapid identification of *Sh. sonnei*. Rectal swabs or faeces were inoculated on desoxycholate citrate medium and incubated for 14 to 18 hours. If sufficient growth was obtained, direct slide agglutinations of suspicious colonies were undertaken with *Sh. sonnei* phase I and II antisera; in some instances positive isolations were made in this manner. Failing a positive slide agglutination, or if insufficient growth was obtained, suspicious colonies were inoculated in Kligler's iron agar medium and 1% mannitol peptone water. After 14 to 18 hours' incubation, slide agglutinations with *Sh. sonnei* antisera were carried out with growth from the Kligler medium. In all instances the plates and Kligler medium were refrigerated and subsequently returned to the central laboratory for complete biochemical and serological investigation by means of the methods described by Cooper (1958). In the later

stages of the epidemic, most specimens were obtained on Stuart swabs and returned to the central laboratory for full examination; such swabs allowed the survival of enteric pathogens for many weeks and thus obviated the necessity for rapid transport and investigation (Cooper, 1957).

With the assistance of the District Health Inspector all past patients, present patients and their contacts were examined bacteriologically. In addition, all food

TABLE II.
Incidence of Known and Suspected Cases of *Shigella Sonnei* Infection During Outbreak.

Age Group.	Number of Cases.	Percentage.
Adult	126	39.5
School age ..	88	27.4
Pre-school age ..	107	33.1

handlers in the township were investigated. Table III records the isolations of *Sh. sonnei* that were made during the survey; no other enteric pathogens were isolated by either the emergency laboratory or the central laboratory during the course of the outbreak. In Table IV the number of bacteriologically proven cases (and contacts) in the various age groups is compared. These figures show considerable differences from those recorded in Table II; it is evident that while the majority of reported cases occurred in adults and pre-school-children, the bulk of the positive isolations occurred in school-children. The significance of this finding may be somewhat open to doubt, but it tends to support the views expressed on the possible mode of spread of infection in the community (*vide infra*).

TABLE III.
Isolations of *Shigella Sonnei* during the Outbreak.

Groups Examined.	Number of People Examined.	Number Excreting <i>Sh. sonnei</i> .
Past, present patients ..	283	39 (13.8%)
Contacts	238	5 (2.1%)
Others, including food handlers	87	0
Totals	608	44 (7.6%)

All strains of *Sh. sonnei* isolated during the outbreak were tested for their sensitivity to various antibiotics with "Sentests" (Evans). With one exception, all strains were highly sensitive to "Chloromycetin", streptomycin, "Terramycin", tetracycline and sulphonamides; the single exception was found to be sensitive only to "Chloromycetin" and streptomycin.

Clinical Findings.

As is generally found in widespread outbreaks of bacillary dysentery, a marked variation in clinical symptoms was observed. The symptoms varied from a mild diarrhoeal episode, apparently experienced by a large proportion of the population, to acute dehydration and shock. The following case histories serve as an indication of the range of symptoms observed during the course of the epidemic.

CASE I: A male patient, 18 years old, was seen on April 12. During the previous night he had passed copious watery brown motions and finally had collapsed unconscious at the door of the outside lavatory. When seen he had recovered consciousness, his temperature was 100.4° F., his pulse rate was 154 per minute and his blood pressure 84 mm. of mercury (systolic). On admission to hospital the patient was given an intravenous transfusion of two litres of

Hartmann's solution over the first two and a half hours, followed by 4% dextrose in 0.2 normal saline. Fluids were taken well by mouth, and phthalylsulphathiazole was given, 2 grammes *statim* and 1 gramme every four hours. Recovery was rapid, and the patient was discharged three days later. No pathogens could be detected in a rectal swab examined three weeks later.

CASE II: A male patient, aged three and a half years, was admitted to hospital on April 15. He had a 24 hours' history of coughing, wheezing and fever. Twelve hours before his admission to hospital he had vomited twice, and had then passed a large, pale, blood-flecked, mucousy stool. Four similar stools were passed prior to his admission. On examination of the patient, his temperature was 102.8° F., his pulse rate was 136 per minute. He had scattered râles and rhonchi throughout both lungs and bronchial breathing at the base of the right lung. The child was treated with forced oral intake of fluids (4% dextrose in 0.2 normal saline), 250,000 units of procaine penicillin daily and chloramphenicol by mouth, 250 mg. *statim*, 125 mg. every four hours. The patient's hydration and chest signs rapidly improved and his diarrhoea decreased, and he was discharged from hospital on April 19. *Sh. sonnei* was isolated from a stool collected on April 15, while no pathogens were detected in rectal swabs examined three and six weeks later.

TABLE IV.
Bacteriologically Proven Cases of *Shigella Sonnei*.

Age Group.	Number of Patients.	Number of Patients with <i>Sh. sonnei</i> .	Bacteriologically Proven.	Percentage of Total Isolations.
Adult	126	11	8.7%	25.0
School age ..	88	22	22.7%	45.5
Pre-school age ..	107	14	13.0%	29.5

CASE III: A female patient, aged eight years, was admitted to hospital on April 22 with pyrexia of unknown origin. She had become ill 12 hours previously, and had vomited twice in that time. On examination of the patient, her temperature was 103.8° F., her pulse rate was 122 per minute, and she was prostrated with photophobia and some neck stiffness. Dry retching continued for five hours, and she then passed a large green, watery, offensive-smelling stool. Three similar motions were passed in the next hour. Fluids given by mouth were tolerated well, and she was treated with chloramphenicol by mouth, 125 mg. *statim* and every four hours. Bacteriological examination of the child's stools collected on April 22 revealed *Sh. sonnei*. The child was discharged from hospital four days later; she and her family were treated with phthalylsulphathiazole, 1 gramme every six hours, for one week. Four weeks later the child's stools were still mucousy and *Sh. sonnei* was again isolated. After a five-day course of streptomycin given by mouth, 1 gramme daily, her symptoms cleared, and two subsequent rectal swab examinations at weekly intervals did not reveal the presence of *Sh. sonnei*.

CASE IV: This is the case of the X family. The first patient, A.X., a girl, aged four years, was admitted to hospital on April 23; she was passing blood-stained watery stools. Fluids by mouth and chloramphenicol (125 mg. every six hours) were given, and the child recovered rapidly, being discharged from hospital two days later. The second patient, B.X., a male, aged 29 years, father of A.X., developed mild

diarrhoea on April 25. Phthalylsulphathiazole (1 gramme every four hours) was given, and his symptoms rapidly subsided.

On May 16, rectal swabs from the foregoing patients, and from the remainder of the family (Mrs. B.X. and two other children) were examined bacteriologically. *Sh. sonnei* was isolated from all five members of the family.

Before the completion of the bacteriological examinations, Mrs. B.X., aged 24 years, complained of continual vomiting with frequent diarrhoea for the past 24 hours. On May 20 she was admitted to hospital in an extremely shocked condition. On examination of the patient, her temperature was 99.8° F., her pulse rate 144 per minute and her blood pressure 70 mm. of mercury (systolic) in the Trendelenburg position. Three litres of Hartmann's solution were given intravenously over four hours. She was treated with streptomycin (1 gramme per day by mouth) for five days, and recovered rapidly.

C.X. and D.X., the two youngest children of the family (aged respectively 10 months and two and a half years), developed slight vomiting and diarrhoea at the same time. They responded rapidly to streptomycin given by mouth.

Rectal swab examination of the entire family after a five-day course of streptomycin by mouth did not reveal the presence of *Sh. sonnei*.

The foregoing case histories broadly indicate the range of symptoms observed during the course of the epidemic. These could be classified roughly into five clinical groups: (i) mild to moderate diarrhoea; (ii) severe and "colicky" abdominal pain with considerable diarrhoea; (iii) shock due to loss of, and failure to assimilate, water and electrolytes; (iv) constitutional symptoms, including pyrexia and prostration; (v) secondary infection, mainly bronchopneumonia (in young children).

A striking feature during the outbreak was the different clinical picture observed in various age groups. As may be seen in Table V adults and pre-school-age children were possibly more severely affected than school-children and infants under the age of 12 months. This feature is not generally observed in shigellosis, infants and younger children usually being the most severely affected. Certainly it was found here that infants were least affected; in the pre-school-age group secondary infection, primarily bronchopneumonia, was most common, and these symptoms tended to weight the severity of infection in this particular section of the community.

In general, three forms of chemotherapy were used in the treatment of cases. These included sulphonamides given orally (phthalylsulphathiazole and succinylsulphathiazole), streptomycin and chloramphenicol; the particular chemotherapeutic agent used depended largely upon the clinical condition of the patient. In most instances, patients mildly affected were treated with sulphonamides, while those sufficiently ill to be admitted to hospital were treated with streptomycin and chloramphenicol. After the establishment of the emergency bacteriology laboratory all patients and all carriers of *Sh. sonnei* detected were treated with a five-day oral course of streptomycin. All patients who had received chemotherapy, in some form or other, were subsequently examined for the presence of *Sh. sonnei*. Table VI records the results of bacteriological examination after

TABLE V.
Variation in Clinical Symptoms Observed During the Outbreak.

Severity.	General Symptoms Observed.			
	Adults.	School Children.	Pre-school Children.	Infants.
Mild ..	"Colicky" pains, loose motions.	Colicky pains, loose motions.	Loose motions.	"Lime-cordial" stools.
Moderate ..	Pain, watery brown stools, mucus.	Vomiting, diarrhoea with occasional blood-stained, mucousy stools, slight pyrexia.	Vomiting, diarrhoea, blood-stained stools, large amount of mucus, some pyrexia.	None observed.
Severe ..	Vomiting, diarrhoea, shock, toxæmia.	None observed.	Vomiting, diarrhoea, pyrexia, secondary bronchopneumonia.	None observed.

the initial treatment of the patients or carriers. Rectal swabs were examined between one and two weeks after the completion of the course of treatment in all instances. There seems no doubt from these results that oral streptomycin therapy was the most successful means of eliminating the organism. It is interesting to note that, while the organisms isolated from all except one of these patients were sensitive to chloramphenicol and sulphonamides, these substances failed to eliminate the pathogen in a substantial proportion of the cases. After the initial treatment, all patients continuing to excrete *Sh. sonnei* were given a further five-day oral course of streptomycin. Rectal swabs examined one week and three weeks after the completion of this treatment were found, in all instances, to be free of the organism.

TABLE VI
Clearance of *Shigella Sonnei* after Chemotherapy.

Drug.	Number of Patients Treated.	Number of Patients Excreting <i>Sh. sonnei</i> after Treatment.
Sulphonamide ..	71	23 (32.4%)
"Chloromycetin" ..	47	5 (10.2%)
Streptomycin ..	39	1 (2.7%)

In the initial period of the epidemic, sulphonamides (usually phthalylsulphathiazole) were used as a prophylactic measure; when a case was reported, all the family contacts were requested to begin a course of the chemotherapeutic agent. It was particularly difficult to assess the success of this measure owing to the large number of people treated in this way. However, on the evidence of reliable patients, it seemed that such prophylactic measures were largely unsuccessful, as a considerable number of them subsequently became infected with the organism.

Epidemiology of the Outbreak.

The immense proportions of this outbreak precluded any detailed study of the pathways of infection within the community. Nonetheless, a number of features which almost certainly were associated with the spread and perpetuation of the outbreak became evident during these investigations.

The initial site of infection occurred at the "shanty town" attached to "F's" mill; a second group of cases, in school-children and infants, then occurred in the "shanty town", and also in a housing community established for mill workers and situated in the town itself. The children infected in this second group were related to one of the earlier patients, and adequate chances for direct transfer of the organisms had apparently occurred. The infection then spread from these two areas throughout the township in a seemingly haphazard manner. However, it was evident at this stage that these infections were occurring in school-children and/or their younger siblings. As one of the children in the second group of cases attended the Mansfield State School, it seemed likely that many of the later infections arose by contact in the school.

Later the infection apparently occurred more frequently in adults than in children, and it is almost certain that many other sources of infection arose during this period. It is interesting to note that, of the 321 known cases, 217 (67.6%) occurred in family groups—that is, two or more persons living in the same household were infected. A total of 69 families were found to have had infections, and of these 62 (89.9%) had children who were either attending school or had adequate contact with other school children. Support for the assumption that the State school was one of the original sources of infection was given by the following facts:

1. It was learned that one of the school-children had become incontinent of faeces, passing a semi-liquid diar-

rhoeal stool at her desk. The teacher and several classmates "cleared-up" after this accident. Six of the child's immediate classmates succumbed to the infection within the next two days, while the teacher developed symptoms three days later. There was no doubt of the source of these particular infections.

2. The toilet facilities at the school were primitive; a pan service was provided, there being 12 closets provided for some 300 children. When the toilets were inspected early in the epidemic, it was quite obvious that the once-weekly removal of the pans was quite inadequate for the demands. Samples taken from the pans were examined bacteriologically, and yielded a heavy growth of *Sh. sonnei*. It was obvious that these lavatories might serve as a considerable source of infection. Moreover, the extremely large fly population around the lavatories could also act as a means of dissemination of infection through the community.

3. There is also a convent school in the town; here the toilet facilities are extremely good, a septic sewerage system being used. A striking feature of the epidemic was that during the first three to four weeks no children from this school, or their parents or younger siblings were notified as suffering from the disease. During the height of the epidemic, however, infections did occur in this group, and it seemed likely that these arose as a result of contact in places other than the school.

It was obvious that, while the school might have served as an initial source of infection in the community, many other sources arose later. Direct contact between patients and other members of the family, the close relationship between many families in the town, and contact at work and other places of meeting all provided means for the direct transfer of the organism throughout the community. In addition, the extremely poor toilet facilities provided for the majority of homes undoubtedly increased the chances of indirect transfer via fomites, including the toilet pans and seats, wash-basins, towels, etc. The pattern of the epidemic—namely, the haphazard spread throughout the town—did not suggest that the water, food or milk supplies would serve as sources of infection, and bacteriological examination of the water and milk indicated a relatively high degree of purity, with no evidence of faecal contamination. Rectal swab examinations of all food-handlers in the town were carried out, but none was found to be carrying *Sh. sonnei*; in retrospect, it was believed that some of these people had had some diarrhoeal symptoms, but had failed to report them. However, there was no evidence to suggest that contaminated foods served as a major source of infection.

There were a number of factors which possibly contributed to the development of the epidemic. Probably the chief of these was the climatic conditions which prevailed at the time; during the epidemic a particularly warm, dry autumn was experienced, with maximum day temperatures of 80° to 85° F. This dry weather undoubtedly encouraged an abnormally large fly population to develop, and it seemed likely that this contributed to the spread of the infection in the community. Allied to this were the extremely poor sewerage and drainage systems in the town. A pan service was used by the majority of homes, while in those places which possessed septic systems, the effluent more often than not ran into the gutters outside these houses. Waste water also was generally discharged into the streets. Here the water stagnated and naturally provided admirable sites for the establishment of large fly colonies. The night-soil disposal also left much to be desired; the disposal site was not far distant from the township and was poorly maintained. The fly population here was enormous, and it was obvious that such flies had easy access to the township.

Possibly one other contributory factor was the extreme apathy of the townspeople who, for some time, stoically accepted the epidemic. Only after considerable encouragement by addresses and discussions at various meeting places was it possible to gain the full support of the community in attempting to control the outbreak.

It could not be claimed that any of the measures adopted throughout the epidemic were eventually successful in controlling it; the arrival of heavy rains and cooler weather, the final appreciation by the community of the seriousness of the epidemic and the need for strict measures in personal hygiene, together with the bacteriological control of all patients and carriers, all more or less coincided and probably all contributed to the cessation of the epidemic. Since then no further cases of *Sh. sonnei* infection have been recorded; nonetheless, it is very likely that the occasional persistent carrier of the organism may exist in the community and serve as a potential source of further infection.

One of the main aims in reporting this outbreak has been to illustrate the problems that may occasionally arise from infections due to members of the *Shigella* genus. The possibility of similar outbreaks in other communities which in many respects resemble Mansfield cannot be overlooked; in fact, a large outbreak of shigellosis recently occurred in Alice Springs, which apparently bore many similarities to those reported here (Campbell, personal communication). While the immediate diagnosis and bacteriological investigation of any enteric infection, and the application of effective prophylactic measures at this stage, would undoubtedly be of great value, the eventual elimination of such infections depends largely upon the personal cleanliness and hygiene of the population, and upon the provision, in all communities, of satisfactory toilet and sewerage facilities.

Summary.

1. An outbreak of *Sh. sonnei* infections involving 321 known cases occurring over a period of six weeks is reported.

2. A wide range of symptoms was observed in patients, ranging from extremely mild diarrhoea to severe prostration, pyrexia and dehydration. As a general rule, adults were more severely affected than children, although secondary infections were more commonly observed in young children.

3. Several forms of chemotherapy were used. Oral streptomycin therapy was found most effective in eliminating infection from both patients and apparently healthy carriers.

4. Certain epidemiological features of the epidemic are discussed, and the possibility of epidemics in townships similar to Mansfield is stressed.

Acknowledgements.

The writers would like to express their appreciation of the untiring efforts of Mr. E. S. A. Wing, District Health Inspector, during the epidemic. They were very grateful for facilities provided for them by Dr. L. E. Vine and Matron J. S. Dodemaide of the Mansfield District Hospital. Finally, their thanks are due to members of the Public Health Laboratory staff for their assistance in the bacteriological investigations which were carried out during and after the epidemic.

References.

- COOPER, G. N. (1958), "Shigellosis in Victoria", *MED. J. AUST.*, 2: 770.
COOPER, G. N. (1957), "Prolonged Survival of Upper Respiratory Tract and Intestinal Pathogens on Swabs", *J. clin. Path.*, 10: 226.

WATCHING AN ECLIPSE OF THE SUN.¹

By JAMES A. F. FLYNN,
Sydney.

ON April 8, 1959, an eclipse of the sun was visible in Australia. One hundred and seventy people, chiefly school-children, who looked directly at the eclipse, had the sight in one or both eyes permanently impaired to some extent. These 170 patients were examined by various ophthalmologists throughout Australia. Of the patients, 40%

estimated that they looked at the sun for not more than 10 seconds. The damage is due to the sun's burning the most important part of the retina. The sight is usually

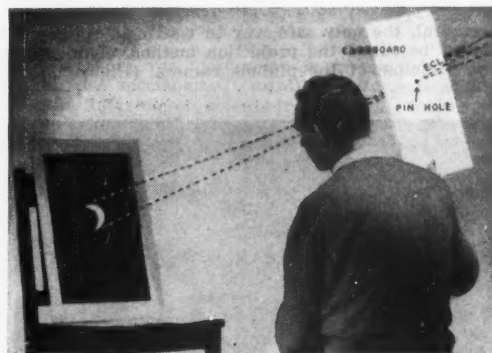


FIGURE I.

Projection method of watching an eclipse. For clarity of illustration, the sun's image has been enlarged and the portion of the cardboard in shadow shown blacker.



FIGURE II.

Watching with a 0.125 in. hole and a distance of five feet.

recovered somewhat when the oedema subsides, but not completely. There are no filters generally available through which it is safe to view an eclipse directly. Of those who suffered damage to their eyes, some wore ordinary sun or glare glasses (one boy even wore two

¹ This paper has been endorsed for publication by the Ophthalmological Society of Australia. Further, this Society has advised the National Health and Medical Research Council that if the educational authorities do not wish to explain this approved method of viewing an eclipse, then children should be instructed not to look at it at all; if it occurs in school hours, they should be kept in class rooms engaged in some work under supervision.

The Government astronomer at Sydney Observatory states that the next eclipse of the sun visible in Australia will take place on March 27, 1960. This will be visible during the hour before sunset in the eastern States, but in Perth it will begin at 3.36 p.m.

pairs); others used photographic negatives (two boys each used three thicknesses); others again used sooted glass, "blue oxy-welder's goggles", "welder's glasses", a dark red globe as used for dark-room photography, a broken beer bottle.

In general, the only safe way to watch an eclipse is by what may be called the projection method. This is based on the principle of the pinhole camera (Figure I). The

For a class of children to view together, make a still larger hole the size of a penny—about 1.2 in. in diameter—and place the white surface about 25 feet away. If the sun is high in the sky, this distance can be obtained

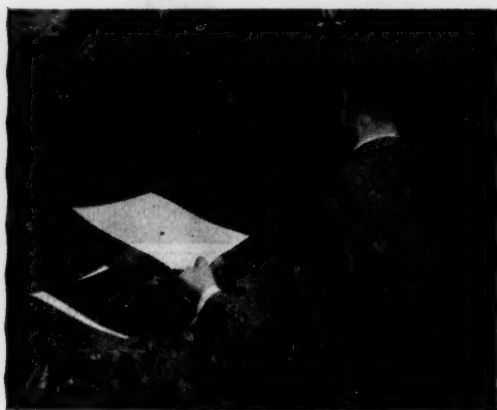


FIGURE III.

Watching with a 0.125 in. hole, but a distance of only one foot. The image is sharp, but rather small.

sun's image is projected on a white surface, and the observer, with his back to the sun, watches the projected image. The image is reversed. The following details are supplied to meet varying requirements:

For individual viewing make a hole with a nail or knitting needle, say 0.125 in. in diameter, in the centre



FIGURE IV.

Watching with a penny-sized hole, but a distance of only 11 feet.

of a piece of cardboard about one foot square, and hold or arrange it at such an inclination that the sun strikes it at right angles and shines through the hole on to a white surface, placed at the same inclination at a distance of about five feet. The image is then the size of a three-penny piece—that is, about 0.6 in. in diameter.

If several wish to view the eclipse together, make a larger hole with a pencil, about 0.3 in. in diameter, and place the white surface about 10 feet away. The image is now about one inch in diameter.



FIGURE V.

An indoor arrangement for watching.

by arranging the card with the hole from an upstairs window or balcony, or on a wall or embankment, and allowing the image to be projected on a white surface on the ground below. The diameter of the image is about 2.75 in. At longer distances the larger holes, by letting through more light, give a brighter image.



FIGURE VI.

The last eclipse as seen by the projection method with a pencil hole at 8 feet (actual size).

It will be seen from the examples given above that the image size increases in proportion to the distance between the hole and the white surface; the shorter this distance, the smaller but sharper the image.

By this simple projection method an eclipse can be watched for its whole duration, not only without danger to the eyes, but with perfect eye comfort and freedom from glare or dazzle (Figures II, III, IV, V, and VI).

It is unnecessary to withhold information concerning a forthcoming eclipse, as has been suggested. Knowledge of the universe is an important part of education, especially in these days of man-made satellites orbiting

in space, and this interesting natural phenomenon can be observed quite safely in the way recommended. It was distressing to find that so many had damaged their sight through ignorance during the recent eclipse, and, more distressing, that a few had done so through disobedience or bravado.

Sight is a precious thing.

A BACKWARD GLANCE AT THE RHEUMATIC DISEASES.¹

By J. F. DREW,
Adelaide.

Yet the patient—the really pitiable patient—has already quite enough to bear from the effects of his complaint and really should not have to suffer still further harm from the physician's ignorance.

So spoke Dr. William Bionnius of the University of Paris in his "Book on Rheumatism", written 400 years ago, and probably the first work devoted entirely to the rheumatic diseases. Today we are so hemmed about with theories of aetiology, so inundated with new and unproved drugs, so bewildered with the biochemical niceties of systemic reactions, that a great degree of nihilism has sabotaged our thinking with regard to the treatment of rheumatism; and should we perchance cry to the physiotherapist for help, as like as not he will reply with inaudible sound. In this scientific maze it is little wonder that both patient and doctor are lost—the former in mournful resignation, the latter in the ever-changing structure of the steroid ring. Faced with such a situation, it is perhaps a comfort to the soul to glance back and retravel the great main road of our long journey. By such an experience we may hope to reorientate ourselves—to gain fresh faith from the past, and, perchance, hope for the future.

GROWTH OF KNOWLEDGE OF RHEUMATISM.

Arthritis can boast an antiquity which stretches into the dim mysteries of the past. It is a ubiquitous disease, and antedates the history of mankind. The British Museum shelters skeletons of prehistoric mastodons and other creatures showing typical arthritic changes, while fossils hundreds of millions of years old show evidence of the disease.

The skeleton of the Neanderthal man of La Chapelle, who, maybe, browsed arboreally 40,000 years B.C., shows marked spondylitis of the cervical and dorsal segments of the spine.

Arthritic changes are seen in the bones of the Neolithic era 10,000 years B.C.

Egyptian mummies of the era 3000 years B.C. exhibit evidence that arthritic disease plagued that ancient civilization much as it does ours today; and, indeed, in the oldest medical textbook preserved, the Ebers Papyrus—written about 1550 B.C.—rheumatism is described, and ointments are recommended "to make the joints limber".

However, it was probably not till the fifth century B.C. that the study of rheumatic diseases reached the stage of differentiation. About that time Hieron of Syracuse recognized podagra (gout) as a distinct type of rheumatic disease. Hippocrates (460-370 B.C.) confirmed these findings and described gout and rheumatism in words that were to influence the medical world for 2000 years.

Apart from the general term "arthritis", which was coined by Galen in the second century A.D. to cover all rheumatic diseases, no further notable advances were made in the knowledge of non-gouty arthritis till the nineteenth century. Sir Arthur Garrod of England introduced the

term "rheumatoid" arthritis in 1859 to differentiate certain forms of rheumatism from rheumatic gout, and in 1872 Weichselbaum of Vienna first sharply divided degenerative joint disease from other arthritides, and accurately described the gross and microscopic anatomy of osteoarthritis.

GOUT.

Whether gout was more common in the olden days, or whether the spectacular nature of the classical disease drew the interest of scientists from the more prosaic chronic rheumatism (even as it does today), is not clear, but more fruitful investigation did take place with gout than with the other rheumatic diseases. Hieron in the fifth century B.C. noted the similarity of gouty tophi and bladder stone. In the fourth century B.C. Hippocrates pointed out the association of alcohol and rich living with gout, and noted the familial tendency. Aretæus of Cappadocia in the second century A.D. described the male preponderance in the disease. Alexander of Tralles (sixth century A.D.) discovered colchicine extract, and this was popularized in the treatment of gout by Gilbert in the thirteenth century, though it was not till 1820 that Pelletier and Caventon isolated the pure alkaloid. In 1787 Wallastom showed that tophi contained uric acid, and six years later Forbes put forward the hypothesis that a higher percentage of uric acid was present in the blood of gouty people.

It was not until some 50 years later (in the middle of the nineteenth century) that this theory was proved by the masterly "uric acid thread experiment" of Garrod. This analysis consisted of placing a cotton thread in three to four ounces of the patient's whole blood and allowing it to remain undisturbed for several days. By weighing the urate crystals adhering to the thread, he was able with reasonable accuracy to estimate the uric acid percentage in the circulating blood. Half a century later still (in 1900), uric acid was classified as a purine body by Fischer. So at the beginning of the twentieth century gout was well known and its association with a raised blood uric acid level realized, Osteoarthritis was clearly distinguished from other forms of joint disease, and Sir Archibald Garrod of England had accurately described rheumatoid arthritis, osteoarthritis, spondylitis deformans, infective arthritides, intermittent hydrarthrosis and metabolic joint disease.

Have we reason to boast of any great advance in our knowledge of these diseases during the last half century?

TREATMENT THROUGH THE AGES.

It is apparent from ancient writings that the treatment of rheumatic disease was well established in Hippocratic and pre-Hippocratic times. It consisted basically of physical medicine in the form of sun-baths and exercises, counter-irritation, and elimination by purging, vomiting, sweating and bleeding. The only drugs given internally in this era were those which produced purging or vomiting, though combinations of herbs to form irritant plasters were in common use.

Greek and Roman medicine and, indeed, medicine throughout the metaphysical era after Hippocrates veered away from physical medicine in a revulsion against sun worship and everything connected with it. This was in no small measure due to the impact of Christianity, and caused undue emphasis to be given to counter-irritant and elimination treatment.

Some Landmarks in the Treatment of Arthritis During the Dark Ages.

In spite of the narrowness of outlook during the metaphysical era, certain physicians advanced learning and were ahead of their time in their ideas.

Alexander of Tralles (sixth century A.D.) not only discovered crude colchicine, but was probably the first to record the stress syndrome, noting that improper habits of living, such as abuses in eating, drinking, working and sexual relationships, as well as passions such as exaggerated ambition, envy, hatred, fear, greed or anger, were

¹ Presidential address, delivered at the thirteenth annual meeting of the Australian Association of Physical Medicine and Rehabilitation on November 13, 1958, held in Sydney in conjunction with the Pan-Pacific Conference on Rehabilitation.

detrimental to the patient. Of the use of colchicine extract, he remarks that though the remedy is effective "it offends the stomach, upsets the appetite and manure-like morbid products are eliminated by bowel movements". Possibly his greatest advance was the use of warm compresses containing opium and hyoscyamus to ease painful joints.

Paracelsus (a Swiss, 1493-1541) also warned against stress—"four things you should avoid, strong flavoured wines, rich food, anger and women"; but he is chiefly notable for the introduction of several new drugs in the treatment of arthritis, such as gold, sulphur, mercury and antimony, as well as numerous vegetable drugs. He based his treatment on three main principles: (i) internal use of alteratives and eliminants; (ii) external application of soothing compresses; (iii) counter-irritation by means of chemical or vegetable corrosives, assisted by cupping and scarification, with the ultimate use of the red-hot iron in extreme cases. He placed treatment on a more rational therapeutic basis, while largely ignoring the physiological aspects. His writings display a robust optimism rather foreign to modern thought:

Who has filled you with such madness and despair as to believe there is neither drugs nor relief for arthritis? I have achieved cures which were not possible for the physicians with all their books.

English Physicians.

About the same time as Paracelsus flourished, Linacre in England (1460-1524) was translating the ancient medical writings of Hippocrates and Galen, and their concepts made a profound impression.

Sydenham (1624-1689), the first great practical physician of England, reflected these ancient teachings in his treatment, using few drugs and tending to assist nature by physical medicine, vomiting, sweating and purgation. Unfortunately, Sydenham, himself a sufferer from gout, did not believe in the use of colchicine, thus delaying the general introduction of this valuable drug. In this way he may well have altered the course of history, as it is generally believed that if Pitt, Earl of Chatham, had not suffered so grievously in health from gout, for which there was then no suppressive drug, he might have been able to prevent England's disastrous foreign policy, which ultimately led to the loss of the American colonies.

Heberden (1710-1801) is chiefly remembered by his nodes. Salicin was first used in the treatment of arthritis as a substitute for quinine by Elliotson in the early nineteenth century, and MacLagan, a Scot, published the results of such treatment in *The Lancet* of 1876, and is generally given the credit of discovering salicylate.

In the latter half of the nineteenth century, Gowers, Still and Strangeways are noted for their descriptive contributions, and towards the turn of the century Sir Alfred Garrod and his son, Sir Archibald Garrod, played important parts in differentiating the various forms of chronic joint disease, and putting the study of the rheumatic diseases on a firm foundation.

EFFECT OF THE SCIENTIFIC ERA ON THE KNOWLEDGE OF RHEUMATIC DISEASES.

In England the scientific era saw the surgical advance of Hunter and Simpson, and the epoch-making researches of Lister into microbial infection. With this swing from the metaphysical era, the humoral theories of pathology gave way to cellular pathology, dominated by the action of pathogenic bacteria. In rheumatic disease, first the uric acid diathesis (or some other such metabolic by-product of unknown composition) formed a common background for treatment. Later, an infective basis, with its corollary the toxic focus, held the physician's attention. As more exact scientific methods of investigation failed to support any of these ideas, we find by the end of the nineteenth century a definite scepticism of all aetiological theories, which in turn led to discarding of the established empirical treatments, and, ultimately, to a sort of therapeutic nihilism which is only too obviously with us to the present day.

It is a sobering thought when we consider our so-called modern treatment to realize how little we have advanced in basic therapy. We have our systems of physical exercises and diets, which were so well established by the ancient Greeks that Plato remarked of Herodikus that "by a combination of training and dieting he has found a way of torturing first himself and secondly the rest of the world by the invention of a lingering death". We have our infra-red lamps and diathermy machines—the direct descendants of Phœbus Apollo and Odin—our ultra-violet equivalent to the ancient Egyptian god Ra. We are greatly inferior in our methods of counter-irritation, but have some anæmic imitations in histamine ionization and certain ointments. Our basic drugs are still salicylate, gold and colchicum, known respectively over 100, 300 and 1400 years ago, and as yet no one can say with certainty how any of them work. Some modern textbooks still gravely recommend the use of lithium to dissolve urate deposits, and sulphur as an antidote for rheumatoid arthritis, but not as Paracelsus prescribed them: now they must be administered by ion transfer. The stress syndrome so ably discovered in recent years was recognized by Alexander 1400 years ago, and 1000 years prior to that Hippocrates and others noted hormonal abnormalities in arthritides, as evidenced by disturbances of menstruation. Really, all we lack in our modern treatment is a good system of purging and blood-letting, though sweating is still practised in our Turkish baths and high bowel wash-outs are far from unfashionable in some clinics.

Where, then, can we turn for something new and dramatic in our attack on these crippling diseases? Certainly not to the adrenal steroids, whose use in chronic rheumatism is little more realistic than treating an inflamed appendix with the continuous administration of morphine. Possibly the antimalarials will come to our aid, but there again the outlook is entirely experimental. Perhaps the only new treatment which has emerged in the last half-century which is likely to stand the test of time because it is fundamentally sound is the principle of rest and splintage for acutely diseased joints, so ably enunciated by Michael Kelly of Melbourne. But even this is not really new, as articles describing the use of plaster splints for rheumatic joints appeared in both the English and American medical Press well over 80 years ago, and even in the first century A.D. Celsus described a stone hollowed out in the shape of a foot in which painful feet could be held and allowed to recover.

It is indeed a sobering thought to realize that our modern armamentarium is based on empirical treatment that has been in use for better or worse throughout the centuries. Further, while we may smile discreetly at the humoral theories of the ancients, we are in no position to replace them with any other of proved scientific accuracy; and until the day dawns when the riddle of the cause of rheumatism no longer torments us, it would no doubt be more rewarding to glance back and adopt treatments of proved empirical worth, rather than be lost in the maze of modern therapeutic adventure.

CONCLUSION.

I will leave you with three quotations:

1. From Hippocrates, the father of ancient medicine, who remarked 2400 years ago in "On Ancient Medicine":

I do not claim that one should throw overboard ancient medicine as if it did not exist at all, or that its investigations were wrong, if it is not accurate in every detail—but I believe we have to consult it further and admire its discoveries which have been made in spite of much ignorance. For beautiful and right are these discoveries and not arbitrary.

2. From Paracelsus, the father of therapeutic medicine, who said some 400 years ago in "Podagric Diseases": "I shall describe the cure of Podagra according to the best masters of medicine."

3. Finally, from A. G. S. Hill, of the Oxford Region Rheumatic Research Centre, who in introducing a symposium on "The Problems of Rheumatism" in *The Practitioner* for July, 1958, concluded: "It is impossible

on the basis of current theories of aetiology to suggest any alternative to our present empirical approach to treatment."

And yet the patient—the really pitiable patient—has already quite enough to bear from the effects of his complaint and truly should not have to suffer still further harm from the physician's ignorance.

THE USE OF AN INTRAMUSCULAR DEPOT OF IODIZED OIL AS A LONG-LASTING SOURCE OF IODINE.

By K. H. CLARKE,

Physics Department, Peter MacCallum Clinic, Melbourne,

S. F. McCULLAGH,

Department of Public Health, Territory of Papua and New Guinea,

AND

DORA WINIKOFF,

Department of Biochemistry, University of Melbourne.

In the Territory of Papua and New Guinea there occur regions where goitre is very prevalent, and should this condition be shown to be benefited by iodine, its efficient administration could be difficult. The use of iodized salt is precluded primarily by the remoteness of the affected areas and the ruggedness of the terrain. Other forms of self-medication are little suited for use by so primitive a people.

There have been several reports in the literature concerning the effects on the level of circulating iodine of iodized oils and of organic iodine-containing dyes, which are used in certain radiographic procedures, and in some cases these effects appear to have lasted for periods of several years (Hyde and Hyde, 1949; Rapport and Curtis, 1950; Starr *et al.*, 1950; Rogers and Robbins, 1955).

It was therefore suggested by the Territory's Department of Public Health that consideration might be given to the use of an intramuscular depot of an iodized oil as a convenient source of iodine. Such an iodine pool, it was thought, might last many months and could be replenished as required during the medical officer's visits to the region.

It was decided, therefore, to investigate (i) the degree to which iodine is released from an intramuscular depot of iodized oil in a form available to the thyroid, (ii) how large such a depot should be, (iii) how long such a depot would last, and (iv) whether the oil, iodized or uniodized, had any adverse side effects or antithyroid properties in the quantities used.

Investigations have been carried out on eight normal subjects. The chemical determination of plasma protein-bound iodine (I^{131}) and the 24-hour percentage retention of a radioiodine (I^{131}) tracer dose by the thyroid have been used as indices of the release of iodine from the iodized oil depot and its entry into the thyroid.

The 24-hour percentage retention of I^{131} by the thyroid (hereafter called thyroidal retention) is partly dependent on the avidity of the gland for iodine, and will be reduced if the gland becomes saturated or partially saturated with iodine.

Plasma protein-bound iodine (hereafter called PBI) consists mainly of hormonal iodine in the form of thyroxine or tri-iodothyronine loosely linked to the circulating plasma proteins, and the measurement of PBI is regarded as reflecting the functional state of the thyroid gland.

Administration of large doses of iodide or Lugol's solution results in increased values of PBI and reduced values of thyroidal retention, but these indices return to normal limits within a matter of days or weeks. On the other

hand, as mentioned above, X-ray contrast media and certain organic preparations produce effects which last for a considerable time—months or even years. In neither case, however, is such an elevation in the PBI value indicative of an increase in the level of true hormonal iodine. Therefore, the term "PBI" (in inverted commas) is used in this paper to indicate an apparent PBI value obtained under such circumstances.

The degree of breakdown of the iodized oil with the liberation of iodine, and the subsequent elimination of iodine in urine and faeces, is reflected in the changes of values of the indices mentioned above. The return of these indices to pre-treatment levels can be taken, therefore, as an indication that the exogenous iodine depot is being exhausted.

Material and Methods.

The eight normal subjects, six males and two females, selected for this study were student volunteers.

Initially a tracer dose of 15 μ c. of I^{131} , carrier free, was administered orally to each subject and the thyroidal retention was determined. The initial level of PBI was also determined in each case, and these results formed the base lines with which all future results were compared.

Two weeks later three subjects (two males and one female) received 0.5 ml. of iodized oil intramuscularly into the buttock, and three others (two males and one female) received 1.5 ml. of iodized oil. The remaining two subjects (both male) were given intramuscular injections of 0.5 ml. and 1.5 ml. of the uniodized oil respectively and were regarded as controls.

Determinations of thyroidal retention and PBI were repeated five weeks after administration of the iodized or uniodized oil, and subsequently at various intervals for eighteen months or longer. Measurements of thyroidal retention were carried out less frequently than the PBI determinations in order that the total amounts of I^{131} administered might be minimal. Only two I^{131} tracers were given to each of the two subjects who received the uniodized oil, since these were sufficient to show that the oil itself had no significant effect on the measurements.

The total amounts of I^{131} given are considered quite safe, particularly as the quantity taken up by the thyroid was low in the majority of tests. In each subject, as soon as the thyroidal retention began to return to normal, the I^{131} tests were discontinued.

In order to reduce the possibility of errors, the eight subjects were asked to avoid foods with a high iodine content for a few days prior to I^{131} and PBI tests, and to have nothing to eat for the two hours prior to and the one hour following the oral administration of I^{131} .

The iodized oil used in this study was *Oleum Iodisatum*, B.P. (1953) ("Neohydriol", May and Baker), a poppy-seed oil containing 39% to 41% w/w of chemically bound iodine.

The method used for the determination of the thyroidal retention, employing two shielded G10Pb Geiger counters placed laterally to the neck, has been described previously (Clarke and Aujard, 1954). The method used for the determination of PBI has also been described (Winikoff, 1954).

Results.

The results are presented in Table I and in Figures I and II.

No adverse side effects of the administration of the iodized or uniodized oil were observed in any of the subjects.

The two subjects who received the uniodized oil showed no significant change in their levels of PBI and thyroidal retention, and it has been concluded that the oil itself has no detectable effect on the metabolism of iodine by the thyroid.

The six subjects who received iodized oil showed early dramatic changes in the level of "PBI" and thyroidal retention. In all cases the "PBI" increased markedly, while the thyroidal retention dropped to low values. The

¹Present address: Diabetic and Metabolic Unit, Alfred Hospital, Melbourne.

TABLE I.

Values of 24-Hour Percentage Retention of I^{131} by the Thyroid and PBI (Microgrammes per 100 ml.) Before and at Various Times After the Intramuscular Injection of Iodized or Uniodized Oil.

Time of Estimation.	Subjects Receiving 0.5 ml of Iodized Oil.			Subjects Receiving 1.5 ml. of Iodized Oil.			Subjects Receiving 0.5 ml. of Uniodized Oil.	Subjects Receiving 1.5 ml. of Uniodized Oil.
	1: F. ¹	2: M. ²	3: M.	4: F.	5: M.	6: M.	7: M.	8: M.
Before administration:								
24-hour I^{131} retention ..	72%	58%	69%	56%	68%	57%	49%	62%
"PBI"	7.5	5.5	5.5	5.5	5.1	6.1	6.5	5.5
5 weeks after administration:								
24-hour I^{131} retention ..	26%	15%	12%	18%	5%	6%	52%	62%
"PBI"	16.6	25.6	23.1	26.2	30.1	44.3	5.2	5.3
12 weeks after administration:								
"PBI"	17.6	15.1	13.0	26.9	23.3	35.2	5.5	5.1
15 weeks after administration:								
"PBI"						33.0		
17 weeks after administration:								
"PBI"	11.8	9.1	10.6					
19 to 20 weeks after administration:								
24-hour I^{131} retention ..	11%	18%	14%	14%	5%	8%		
"PBI"	13.8	9.9	13.4	17.8	16.3	23.6		
28 to 29 weeks after administration:								
24-hour I^{131} retention ..	9%	9%	9%		2%	2%		
"PBI"	9.6	9.3	9.1		13.6	14.3		
46 to 47 weeks after administration:								
24-hour I^{131} retention ..	14%	21%	14%	2%	9%	7%		
"PBI"	13.1	5.8	9.8	13.4	9.0	10.4		
57 weeks after administration:								
"PBI"	10.9	5.9	7.4	10.8	8.6	10.3		
66 weeks after administration:								
24-hour I^{131} retention ..		22%						
70 weeks after administration:								
"PBI"		6.7						
80 to 85 weeks after administration:								
24-hour I^{131} retention ..	39%		19%		21%			
"PBI"	7.2		6.8	11.0	6.2	9.9		
92 weeks after administration:								
"PBI"				9.2		9.6		
103 weeks after administration:								
"PBI"				8.5		9.6		
115 weeks after administration:								
"PBI"				7.7				
128 weeks after administration:								
24-hour I^{131} retention ..				26%		16%		
"PBI"				9.3		8.0		

¹ F, female.

² M, male.

three subjects who received 1.5 ml. of iodized oil showed appreciably greater changes than those who received 0.5 ml. of iodized oil, and in both groups the changes in indices were smaller for the females than for the corresponding males.

The greatly elevated "PBI" levels, which followed the administration of iodized oil, fell considerably over the subsequent few months, but remained well above the normal range. The general return to normal levels thereafter continued more gradually.

Throughout the whole investigation the decreased values of the thyroidal retention were consistent with the increased levels of plasma "PBI", except that their return to pre-iodized oil levels in all cases was considerably more delayed (Figures I and II).

The initial values of the thyroidal retention, while higher than would be expected in many other centres for normal individuals, are not abnormal for Melbourne.

Discussion.

Intramuscular injections of 0.5 ml. or 1.5 ml. of iodized oil have been given to six normal subjects.

The "PBI" levels of those individuals who received intramuscular injections of 0.5 ml. of iodized oil returned

to normal levels within 11 to 18 months, whereas of the three who received injections of 1.5 ml. of iodized oil, only one had a normal "PBI" value at 18 months and the other two still had high "PBI" levels after two years. The thyroidal retentions, however, were much slower in returning to pre-iodized oil values.

The prolonged reduction of the thyroidal retention after the return of the "PBI" to within normal limits is interesting. The possibility that it represents an inhibition of thyroid function is unlikely, since, throughout the two years of this study, none of the subjects has developed goitre or shown any evidence of hypothyroidism. It is considered that the effect is due to the continued partial saturation of the gland with iodine as the content of the iodized oil depot approaches zero.

Generally the view is held that iodine must be in the form of iodide in order to be trapped by the thyroid, hence it must have been released from the iodized oil either in this form or as a simple metabolite of it, although not necessarily at the site of injection. This point is still under investigation by one of us (D.W.).

It is concluded that an intramuscular depot of iodized oil can provide a long-lasting source of iodine, the duration of the source being dependent on the size of the depot

used. It appears that a 0.5 ml. depot would be sufficient for one to one and a half years, and that a 1.5 ml. depot would be adequate for one and a half to two years, but whether these figures apply to a goitrous population has yet to be determined.

This mode of iodine administration is well suited for use in the control of endemic goitre due to iodine

certain types of endemic goitre do not respond to the administration of iodine (Clements and Wishart, 1956).

It is of interest to note that following a preliminary report of this work at the A.N.Z.A.A.S. meeting in Dunedin, New Zealand, in January, 1957, this method of iodine administration has been employed by several groups of workers studying hypothyroidism in animals, and their

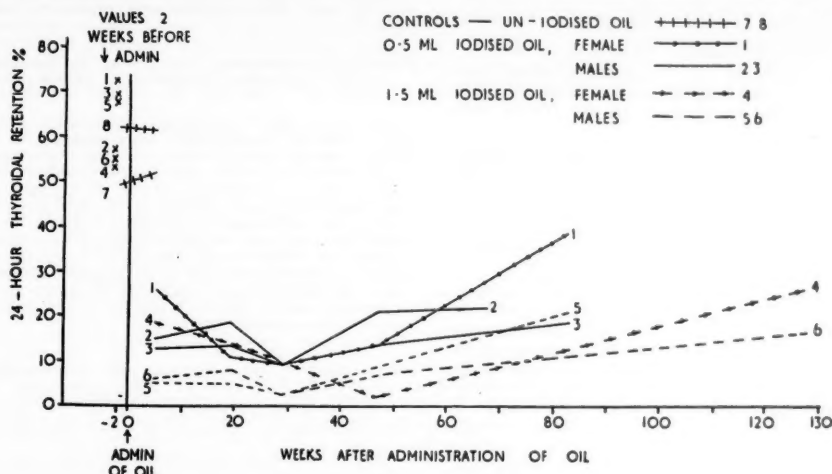


FIGURE I.

The effect of an intramuscular depot of iodized or uniodized oil on the 24-hour percentage retention of I^{131} by the thyroid.

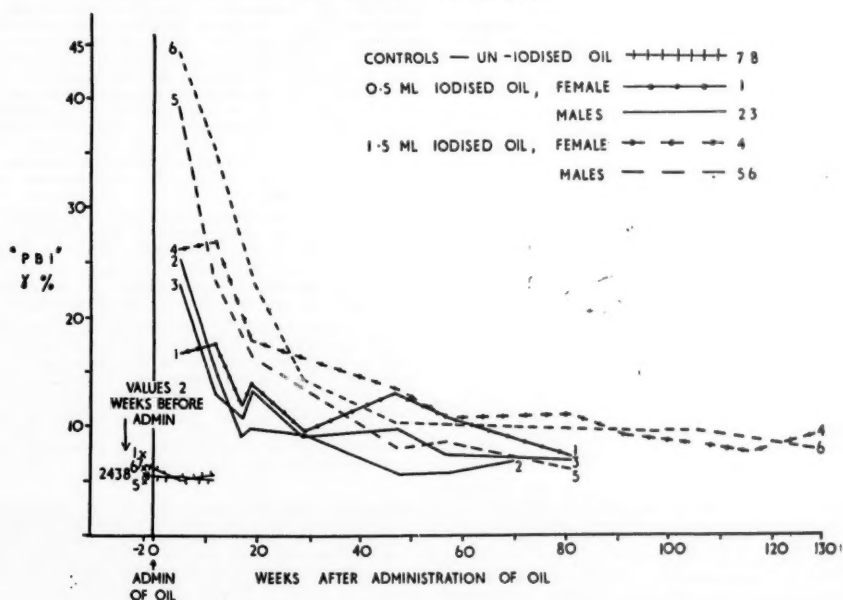


FIGURE II.

The effect of an intramuscular depot of iodized or uniodized oil on the "PBI" values.

deficiency, not the least of its advantages being that it allows selection of those patients who may be given iodine without risk of inducing thyrotoxicosis. No such safeguard exists with the general use of iodized salt.

The administration of iodine by means of intramuscular injection of iodized oil has already been undertaken by one of us (S.F.McC.) in the Territory of Papua and New Guinea, but it is too early at the present time to evaluate its effectiveness. It should be appreciated, however, that

results also indicate that the use of iodinated oil, given intramuscularly, is effective as a source of supplemental iodine. The results of one of these investigations have now been published (Myers and Ross, 1959).

Conclusion and Summary.

The intramuscular injection of iodized oil (B.P.) is a useful and acceptable method of continuous administration of iodine over long periods.

The iodine released from the iodized oil is made available to the thyroid for the synthesis of thyroid hormone. Depots of 0.5 ml. of iodized oil containing 40% iodine w/w appear adequate for one to one and a half years, and depots of 1.5 ml. for one and a half to two years.

There are no adverse side effects resulting from this mode of administration, which appears to be well suited for use in undeveloped areas in an endeavour to control endemic goitre due to iodine deficiency.

Acknowledgements.

We are greatly indebted to Dr. Keith Fairley, who selected the student volunteers and undertook their medical supervision, and who helped in the initial planning of the experiment.

We also wish to thank our respective heads of departments—Dr. J. H. Martin, Physics Department, Peter MacCallum Clinic, Melbourne; Dr. R. F. Scragg, Acting Director of Public Health, Territory of Papua and New Guinea; and Professor V. M. Trikojus, Department of Biochemistry, University of Melbourne—for their interest and encouragement in the pursuit of this study.

Thanks are also due to the student volunteers, without whose cheerful cooperation this investigation would not have been possible, to Miss J. Milne and Miss M. J. Hughes for technical assistance, and to Dr. D. H. Curnow, of the Royal Perth Hospital, Western Australia, for his assistance in carrying out certain tests on one of the volunteers who moved to that State.

References.

- CLARKE, K. H., and AUJARD, R. L. (1954), "Thyroid Symposium III: The Use of Radioactive Iodine I^{131} in the Diagnosis of Hyperthyroidism: Physical Aspects", *Med. J. Aust.*, 1: 891.
- CLEMENTS, F. W., and WISHART, J. W. (1956), "A Thyroid-Blocking Agent in the Etiology of Endemic Goitre", *Metabolism*, 5: 623.
- HYDE, L. R., and HYDE, B. (1949), "Effect of Retained Bronchial Lipidol on Blood Volume", *J. Lab. clin. Med.*, 34: 1516.
- MYERS, B. J., and ROSS, D. A. (1959), "The Effects of Iodine and Thyroxine Administration on the Romney Crossbred Ewe", *N.Z. J. agric. Res.*, 2: 552.
- RAPPORT, R. L., and CURTIS, G. M. (1950), "The Clinical Significance of the Blood Iodine. A Review", *J. clin. Endocr.*, 10: 735.
- ROGERS, W. R., and ROBBINS, L. R. (1955), "Iodipamide (Cholografin Administration), Its Effect on the Thyroid Uptake of I^{131} and the Serum Precipitable Iodine in Euthyroid Persons", *New Engl. J. Med.*, 253: 424.
- STARR, P., PETTIT, D. W., CHANEY, A. L., ROLLMAN, M. D., AIKEN, J. B., JAMIESON, B., and KLING, I. (1950), "Clinical Experience with Blood Protein-Bound Iodine Determination as Routine Procedure", *J. clin. Endocr.*, 10: 1237.
- WINKOFF, D. (1954), "Thyroid Symposium II: Protein-Bound Iodine as Diagnostic Aid in Thyroid Dysfunction", *Med. J. Aust.*, 1: 859.

Reviews.

Nobody Need Be Fat. By R. Kemp, T.D., M.D., M.R.C.P.; 1959. London: William Heinemann Medical Books Limited. 7½" x 4½", pp. 155. Price: 12s. 6d. (English).

THERE seems to be no end to the articles in the medical and lay Press and to books on the subject of obesity and its treatment. Most of the treatments advocated have been found to be relatively useless except in a few cases. The latest book on the subject is "Nobody Need Be Fat" by Robert Kemp. This is a refreshingly straightforward book. More than half of it is taken up with a very interesting account of the nature of obesity, its cause, its dangers and its relation to food and calorie intake, and of methods which have been used for its treatment. The method of treatment used by the author follows on the conception, now widely accepted, that the fat which is laid down in obesity comes from the carbohydrates in the food ingested, and not, to any great extent, from the protein and fat.

The method is to eat a relatively normal diet, except that all foods with carbohydrates, such as sugar, and all foods containing starch, are cut out, and the calorie requirements are made up with extra proteins and fat. Useful menus and recipes are given, and with a little thought the meals can be quite acceptable. In particular there is no cutting down of the amount of food eaten except for carbohydrates.

The author does not claim that every patient treated will show a successful reduction in fat, for the reduction is slow and many people cannot stay the distance. Of 193 patients, the author claims that 40 have achieved complete success, 46 being still under treatment and progressing favourably. The rest of this series of cases were failures, mostly because the patients ceased treatment early.

This is one of the most sensible books that have appeared on the subject of treatment of obesity, and it can be read with interest and profit by both doctor and patient.

Tetanus Neonatorum. By B. A. S. Gerungan, Med. Drs. Arts., Djakarta: Dedicated to World Health Organization. 7½" x 5½", pp. 16. Price: not stated.

THIS is a short pamphlet, apparently published by the World Health Organization in Djakarta, by an Indonesian doctor, giving brief notes on the occurrence of tetanus neonatorum in North and South Celebes, where he states that it is an important cause of infant mortality. He attributes this high incidence to the use of dirty implements, in particular the bamboo knife, in severing the umbilical cord, and to the practice of applying as a dressing a paste of earth and leaves. He states that an important sign of tetanus infection is an almost bloodless cord, which dries up quickly and separates prematurely; this is seen in nearly every case. This is a pamphlet of historical rather than clinical interest.

First Studies in Anatomy and Physiology. By John Cairney, D.Sc., M.D., F.R.A.C.S., and John Cairney, B.Sc., M.B., Ch.B.; Second Edition; 1959. Christchurch: N. M. Peryer Limited. 7½" x 4½", pp. 236, with 105 illustrations. Price: 30s. (New Zealand).

THIS little book appeared three years ago, being intended as a preliminary reader to W. P. Gowland's "Anatomy and Physiology for Nurses" and as a textbook for training midwives who are not already registered general nurses. Actually it can be read easily by a layman, for it presupposes no knowledge of basic sciences. Some elementary aspects of chemistry, biochemistry and biology are discussed in a general introduction, and the succeeding chapters deal, system by system, with the anatomy, physiology and histology of the human organism. There are occasional references to embryology, and all Latin terms used are explained, frequently with derivations. The aim has been to set out clearly and simply some basic principles, to interrelate the subjects and to give an over-all picture on which to base more detailed study. While simplicity is the keynote, the authors have avoided over-simplification—no mean achievement in a work of two hundred pages.

A few criticisms, however, may be made; some sections one feels to be unnecessarily brief, even for a book of this limited scope, especially that dealing with blood groups and the Rh factor. Again, no mention at all is made of genetics, even where a paragraph would be applicable, as in the chapter dealing with reproduction.

The presentation of the book is admirable. Although slight changes in the text have been made in this second edition—namely enlarging of the sections on hormones and vitamins—the big improvement has been the resetting of the type in a more attractive form. Several features facilitate reading and study, including an excellent index, copious use of subheadings and italics, and more than 100 line drawings by the authors, all pertinent, clear and large. In a word, the book is excellent.

Industrial Carcinogens. By R. E. Eckardt, M.D., Ph.D., F.A.C.P.; "Modern Monographs in Industrial Medicine", Editor-in-Chief: Anthony J. Lanza, M.D.; Consulting Editor: Richard H. Orr, M.D.; 1959. New York and London: Grune & Stratton, Inc. 8½" x 5½", pp. 176, with 43 illustrations. Price: \$6.50.

THIS is another of the series "Modern Monographs in Industrial Medicine". The book is a good summary of industrial carcinogens, the criteria necessary for the diagnosis of an occupational neoplasm, and measures of prevention. It stresses, *inter alia*, certain facts of general interest (paying due regard to Percival Pott, who said the first word on the subject in 1775). These are: (i) Occupational cancers are relatively few. (ii) In the past their presence has been suspected as the result of the acumen of practising physicians. (iii) Subsequent experimental work has pin-pointed the offending substance. (iv) In proving the presence or absence of an industrial carcinogen, an epidemiological-statistical approach is necessary. (v) Industrial neoplasms are amenable to pre-

vention. (vi) Of all occupational neoplasms, 75% affect the skin and 15% the bladder, and nearly all the remaining 10% are found in the respiratory tract. (vii) Altogether there are 18 known occupational causes of cancer—including a relatively new one found in the manufacture of isopropyl alcohol.

This monograph, which is well presented, would be of interest to most practitioners, and very useful to those confronted with compensation claims alleging an occupational cause for a cancer. However, it is too briefly presented for specialists in the field of research or industrial medicine, and the scant treatment given to ionizing radiation, ultra-violet radiation and atmospheric industrial contaminants is disappointing. The bibliography is excellent.

Atomic Medicine. Edited by Charles F. Behrens, M.D., F.A.C.R.; Third Edition; 1959. Baltimore: The Williams and Wilkins Company. 9" x 6", pp. 720, with many illustrations. Price: £8 5s.

The third edition of this book follows six years after the appearance of the second edition, which was compiled largely by medical men in response to the insistent problem, "The Atom Knocks at the Doctor's Door". Although there have been many new developments in this wide field since 1953, the editor, although introducing new subject matter as well as coping with scientific progress, has managed to add no more than 100 pages to the text. The best example of incorporation of new material is the chapter on pre-radiation and post-radiation protection, which brings advances in knowledge in this subject up to 1956. It is regrettable that the work of Bacq and Alexander, although not entirely overlooked in the text, is not given as a reference at the end, where those seeking information would be best rewarded by a list of their works. There are now over 200 pages devoted to the biological and medical applications of radioisotopes, over half the subject matter being contributed by Geschickter and Copeland.

Although this is difficult to achieve when a text is compiled by so many authors—albeit expert in their fields—overlap of material does not intrude. However, the units of radiation measurement are defined quite fully in two places. In this connexion there may be lingering doubts concerning the definition of the rem on page 311, where it is stated that this unit is biologically equivalent to 1r. Immediately preceding this definition it has been stated that for practical purposes of radiation safety, the difference between the rad and the rep is negligible. This is certainly not the case when the rem is being derived for the purpose of measurement of exact dosage, and this should have been emphasized. It would seem unnecessary and tedious, and misleading in this instance, to repeat these physical measurements, which could be adequately dealt with in the chapter on detection and measurement. There is a sensational proof-reading error at the foot of page 47.

This is an adequate continuation textbook of nuclear and atomic medicine, a branch of medicine which is related most to radiology, but whose origin stems from many disciplines. An idea of its appeal could best be given by the vocations of the contributors in descending order of the magnitude of their contributions. It is largely written and edited by a radiologist. Then there are medical graduates whose interest is radiation medicine, radiobiologists, biophysicists, biochemists, pathologists, a nuclear physicist and a dentist. The work is also of great value to civil defence workers, to the services and to those interested in preventive medicine.

Antibiotics Annual, 1958-1959. Edited by Henry Welch, Ph.D., and Felix Marti-Ibanez, M.D.; 1959. New York: Medical Encyclopedia, Incorporated. 10" x 6", pp. 1128, with many illustrations and tables. Price: \$12.00.

The sixth annual symposium on antibiotics was held in Washington in October, 1958, and in accordance with well-established custom its proceedings are published as the latest "Antibiotics Annual". It opens with a group of important historical papers. The moderator of this symposium was Dr. Felix Marti-Ibanez, and the speakers were Sir Howard Florey, who discussed coric penicillin in perspective, Dr. Selman Waksman, who spoke on "Antibiotics of Actinomycetes, an Introduction and an Outlook", Dr. Chester S. Keefer, who discussed "The Impacts of Antibiotics on American Medicine", and Dr. Harry F. Dowling, who considered "The History of the Broad Spectrum Antibiotics". Then follow approximately 175 papers of varying length on recent investigations and experiences with antibiotics. To conclude the volume are two panel

discussions. One deals with the current status of erythromycin, kanamycin, novobiocin, oleandomycin, ristocetin and vancomycin, with particular reference to their use in staphylococcal disease. The other deals with the causation, prevention and control of staphylococcal diseases in hospitals. Subject and author indexes help to make accessible the vast amount of new material in this volume. It may be expected to have a large and interested medical public.

Abnormal Hemoglobins. A symposium organized by The Council for International Organizations of Medical Sciences, edited by J. H. P. Jonxis and J. F. Delafresnaye, C.I.O.M.S., Paris; 1959. Oxford: Blackwell Scientific Publication. 8½" x 5½", pp. 440, with many illustrations. Price: 45s. (English).

This book reports the proceedings of a symposium on "Abnormal Hemoglobins", organized by the Council for International Organization of Medical Sciences, and held at Istanbul in September, 1957. It is divided into two roughly equal sections, the first on "Biological Considerations" and the second on "The Geography of Hemoglobins". There are 26 papers, all by active investigators, many of whom are leading authorities in their fields; the general discussion on a number of the papers is included. The papers discuss all the various aspects of the hemoglobinopathies—biochemistry, genetics, clinical aspects, geographic distribution and relationship to other diseases.

At the end of the book is a helpful summary of the conclusions of the meeting. The first paragraph of this summary succinctly sums up the importance of studies on abnormal hemoglobins as follows:

The work done to date in the field of abnormal hemoglobins is of great importance not only to biochemists and geneticists but also to physicians, anthropologists and to those who are concerned with the health of the populations of certain regions of the world. In many countries abnormal hemoglobin synthesis affects the infant mortality rate, the malaria mortality rate and the health of large numbers of people. Investigators who study hemoglobin levels, splenic pathology, kidney function and states of malnutrition in certain regions of the world should bear in mind that the presence of abnormal hemoglobins may influence their results. Further studies of fetal hemoglobin levels at the time of birth are desirable because it may be possible to determine new standards for maturity.

Australian physicians and clinical pathologists have recently become interested in the hemoglobinopathies, because of the number of migrants from Italy and Greece who have arrived in Australia since World War II. Thus they will be particularly interested in the papers on "Clinical and Hematological Aspects of the Various Hemoglobin Syndromes" by Zuelzer, "The Distribution of Microcythæmias (or Thalassæmias) in Italy" by Silvestroni and Bianco, and "Hereditary Anemias in Greece" by Fessas.

The book is well produced and edited. It will be warmly welcomed by all persons interested in the hemoglobinopathies.

Hematological Technique for Medical Laboratory Technicians and Medical Students. By E. M. Darmady, M.A., M.D. (Camb.), F.R.C.P., and S. G. T. Davenport, F.I.M.L.T.; Second Edition; 1958. London: J. and A. Churchill, Limited. 9½" x 6", pp. 264, with four coloured plates and 23 text figures. Price: 24s. (English).

In this edition, the subjects of blood-bank organization and parasitology have been omitted, but several additional techniques—notably for the Rose-Waaler test, electrophoresis of hemoglobin and the investigation of hemorrhagic disorders and four new chapters on hospital serology have been included.

As in the earlier edition, it is apparent that it is not easy to combine clarity and accuracy with brevity in the explanations that the authors have attempted of the theoretical background of the laboratory procedures described. For instance, there is ambiguity in the last sentence of the following statement (page 126): "Two diseases of infective origin not only give an absolute lymphocytosis but also abnormal forms. These are glandular fever, or infective mononucleosis, and virus pneumonia. Both may be present in a number of ways, often in epidemic form."

One cannot accept, as either basically or historically correct, the statement on page 195 that "There were originally six Rh antigens, grouped into three pairs Cc, Dd, Ee".

The depiction of cells in the various stages of erythrocyte maturation in the coloured plates is excellent. It would seem, however, preferable to follow Whitby and Britton in the use of the term "proerythrocyte" for a common progenitor of cells of both normoblastic and megaloblastic development, rather than to describe simply as megaloblasts those cells which, in a later stage of development, are termed "early megaloblasts".

Correction of errors in the text would be advisable in any future edition. It is not clear, for example, why the section on the P antigen is included under the heading "M, N, S, Blood Groups" (page 193), and on page 217 the words "Election of Rh Antibodies" should surely read "Elution of Rh Antibodies".

The descriptions of the technical procedures, their advantages, disadvantages and limitations, are clear and in general suggestive of first-hand experience in the use of those selected for inclusion. The collection in one small volume of such a comprehensive range of the tests which may be called for in the laboratory investigation of hematological problems will probably be found helpful by technicians and others needing such information.

The value of the book is essentially as a practical guide.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Studies on the Epidemiology of Filariasis on Central and South Pacific Islands", by Elton E. Byrd and Lyle S. St. Amant; September, 1959. South Pacific Commission Technical Paper No. 125. New Caledonia: South Pacific Commission. 7½" x 10", pp. 96. Price: 6s. (sterling).

"Expert Committee on Hygiene and Sanitation in Aviation, First Report", World Health Organization Technical Report Series, No. 174; 1959. Geneva: World Health Organization. 9½" x 6½", pp. 64. Price: 3s. 6d.

"Annotated Bibliography of Filariasis and Elephantiasis", Part 4—"Treatment", by M. O. T. Iyengar; South Pacific Commission Technical Paper, No. 124; August, 1959. New Caledonia: South Pacific Commission. 7½" x 10", pp. 190. Price: 6s. (sterling).

"Social Psychiatry and Community Attitudes", Seventh Report of the Expert Committee on Mental Health; World Health Organization Technical Report Series, No. 177; 1959. Geneva: World Health Organization. 9½" x 6½", pp. 40. Price: 1s. 9d. (English).

"Roentgen, Rads and Riddles: A Symposium on Super-voltage Radiation Therapy Held at the Medical Division, Oak Ridge Institute of Nuclear Studies, July 15, 16, 17 and 18, 1956", edited by M. Friedman, M.D., M. Brucer, M.D., and Elizabeth Anderson; 1959. Washington: U.S. Government Printing Office. 10½" x 7½", pp. 510, with many illustrations. Price: \$3.50.

"British Empire Cancer Campaign: Thirty-Sixth Annual Report Covering the Year 1958"; 1959. London: British Empire Cancer Campaign. Part I: The Chairman's Statement and the Accounts. 9½" x 7½", pp. 42. Part II: The Scientific Report. 9½" x 7½", pp. 650, with illustrations. Price: not stated.

"United Nations Relief and Works Agency for Palestine Refugees"; 1959. Beirut: United Nations Relief and Works Agency. 8½" x 6", pp. 38, with illustrations. Price: not stated.

"Miscellaneous Notes (Third Series)", by F. Parkes Weber, M.D., F.R.C.P., F.S.A.; 1959. London: H. K. Lewis and Company, Limited. 7½" x 4½", pp. 8. Price: 2s. 6d.

"The Medical Annual: A Year Book of Treatment and Practitioners' Index", edited by R. Rodley Scott, M.A., D.M., F.R.C.P., and R. Milnes Walker, M.S., F.R.C.S.; seventy-fifth year; 1959. Bristol: John Wright and Sons Limited. Toronto: The Macmillan Co. of Canada Ltd. 8½" x 5½", pp. 655, with illustrations. Price: not stated.

"Sigmund Freud's Mission: An Analysis of His Personality and Influence", by E. Fromm; 1959. London: George Allen & Unwin. 7½" x 4½", pp. 127. Price: 12s. 6d.

"The Very Error of the Moon", by Theodore G. Gray, C.M.G.; 1959. Hifracombe, North Devon: Arthur H. Stockwell Limited. 7" x 4½", pp. 192, with illustrations. Price: 15s. (English).

"Color Atlas and Management of Vascular Disease", by W. T. Foley, M.D., F.A.C.P., and I. S. Wright, M.D., F.A.C.P.; 1959. New York: Appleton-Century-Crofts, Inc. 10" x 7½", pp. 184, with many illustrations. Price: not stated.

"High Blood Pressure and Pregnancy", by Lance Townsend, M.D., B.S., F.R.C.S. (Edin.), F.R.A.C.S., F.R.C.O.G., D.T.M. & H.; 1959. Victoria: Melbourne University Press. 8½" x 5½", pp. 124, with 26 tables. Price: 40s.

"The Physiology and Treatment of Peptic Ulcer", edited by J. Garrott Allen, et alii; 1959. Illinois: The University of Chicago Press. 9½" x 6", pp. 250, with many illustrations. Price: \$7.50.

"Open Reduction of Common Fractures", by Oscar P. Hampton, Jr., M.D., F.A.C.S., and William T. Fitts, Jr., M.D., F.A.C.S.; 1959. Modern Surgical Monographs, editor-in-chief: L. S. Ravdin, M.D.; consulting editor: Richard H. Orr, M.D. New York and London: Grune & Stratton, Inc. 9" x 6", pp. 224, with many illustrations. Price: \$8.75.

"Medical X-Ray Technique: Principles and Applications", by G. J. Van Der Plaats; 1959. Eindhoven, Holland: Philips' Technical Library. Sydney: Philips Electrical Industries Pty. Ltd. 9" x 6", pp. 492, with 213 illustrations. Price: £3 10s.

"The Ciba Foundation for the Promotion of International Co-operation in Medical and Chemical Research: Report for the Years 1949-1959"; 1959. London and Dunstable: Waterlow & Sons, Limited. 4½" x 7½", pp. 64, with illustrations.

"Transmission of Atrial Waves to Peripheral Arteries in Complete Heart Block and Atrial Flutter in Man", by Folke Heyman; Acta Medica Scandinavica, Supplement 344; 1959. Göteborg, Sweden: Typografiska Göteborg. 9½" x 6½", pp. 52, with illustrations. Price: not stated.

"Fluoridation: Errors and Omissions in Experimental Trials", by Philip R. N. Sutton, D.D.Sc. (Melb.), L.D.S. (Vic.); 1959. Carlton: Melbourne University Press. 8½" x 5½", pp. 96, with illustrations. Price: 8s. 6d.

"Smoking: the Cancer Controversy. Some Attempts to Assess the Evidence", by Sir Ronald A. Fisher, Sc.D., F.R.S.; 1959. Edinburgh and London: Oliver and Boyd. 8½" x 6½", pp. 48. Price: 2s. 6d. (Abroad).

"Iron Deficiency Anemia", World Health Organization Technical Report Series, No. 182; Report of a Study Group; 1959. Geneva: World Health Organization. 9½" x 6½", pp. 16. Price: 1s. 9d.

"The Mouth: Its Clinical Appraisal", by A. B. Riffle, D.D.S.; 1959. Philadelphia and Montreal: J. B. Lippincott Company. Sydney: Angus & Robertson, Limited. 7½" x 4½", pp. 128, with 22 illustrations. Price: 38s. 6d.

"Hypnosis: Fact and Fiction", by F. L. Marcuse; 1959. Mitcham, Victoria: Penguin Books Pty. Ltd. 7" x 4", pp. 224. Price: 5s. 6d.

"Blindness in West Africa", by F. C. Rodger, M.D., Ch.M., D.O.M.S., with a foreword by Sir Stewart Duke-Elder, G.C.V.O., D.Sc., LL.D., F.R.C.S.; 1959. London: H. K. Lewis & Company, Limited. 9½" x 6½", pp. 276, with 1 coloured plate, 6 maps and 96 text figures. Price: £3 10s. (English).

"Diagnosis and Treatment of Menstrual Disorders and Sterility", by S. L. Israel, M.D.; fourth edition; 1959. New York: Paul B. Hoeber Inc. 9½" x 6", pp. 678, with illustrations. Price: \$15.00.

"Arterial Embolism in the Limbs: The Clinical Problem and its Anatomical Basis", by A. L. Jacobs, M.A., D.M. (Oxon.), F.R.C.P., with a foreword by C. G. Rob. M.C., M.A., M.Chir. (Cantab.), F.R.C.S.; 1959. Edinburgh and London: E. & S. Livingstone Limited. 9½" x 6½", pp. 212, with 37 illustrations. Price: £1 15s. (English).

"Surgical Treatment of Bone and Joint Tuberculosis", by Robert Road, M.A., M.Ch.Orth., F.R.C.S.Eng., W. H. Kirkaldy-Willis, M.A., M.D., B.Chir., F.R.C.S.Eng., and A. J. M. Cathro, M.B., Ch.B., with a foreword by Harold Boyd, M.D., F.A.C.S. Illustrations by W. Caneel, M.C.S.P.; 1959. Edinburgh and London: E. & S. Livingstone, Limited. 9½" x 6½", pp. 150, with 90 illustrations and 10 tables. Price: £1 10s. (English).

"Soil, Grass and Cancer: Health of Animals and Men is Linked to the Mineral Balance of the Soil", by André Voisin, translated from the French by Catherine T. M. Herriot and Dr. Henry Kennedy; 1959. London: Crosby Lockwood & Son, Limited. 8½" x 5½", pp. 320, with 16 illustrations. Price: 30s. (English).

The Medical Journal of Australia

SATURDAY, JANUARY 16, 1960.

PLACEBO SURGERY.

ONE difficulty in assessing the results of any form of treatment is the natural response of the patient, rather than his disease, to treatment. This has been resolved with respect to drug therapy by the use of the double-blind method of trial, in which the drug to be tested is varied with a control, usually an inert placebo, either on different patients selected randomly, or *seriatim* on the same patient, so that neither the patient nor the prescribing physician nor the assessor is aware of the nature of the treatment until all results have been recorded and the study has been concluded. One sidelight of this type of investigation has been the discovery of the toxic effects of inert preparations in addition to their placebo effectiveness in the relief of symptoms.

Recently the placebo method has been adapted to the surgical sphere with interesting results. In 1955, an Italian group of workers reported favourable results in the treatment of angina pectoris due to coronary artery disease by a surgical procedure in which the internal mammary arteries were ligated through a pre-cordial incision. The rationale of the operation was to increase the blood flow to the pericardial tissues through the pericardial branches of the internal mammary arteries. Several subsequent reports, mainly from U.S.A., suggested that the symptoms had been lessened in a number of patients by this operation, which has no mortality and a negligible morbidity. However, two recent studies from U.S.A.^{1,2} are informative. Patients with intractable angina were prepared for operation; then, at the last moment in the operating theatre, the surgeon opened an envelope instructing him either to ligate the internal mammary arteries or merely to make the incision and explore but carry out no definite procedure. Subsequent follow-up care and observations were in the hands of individuals who did not know or who could not tell what had been done. No one will be greatly surprised by the fact that the patients in the ligated and the non-ligated groups showed little difference in the final

assessment fifteen months later. More revealing is the fact that just over half the patients in both groups reported marked relief of symptoms, increase in exercise tolerance and reduction in nitroglycerine intake six months after the operation. Whilst it may be argued that the assaults were totally unjustifiable, we are obliged to record that half the patients were given six months' amelioration of previous crippling symptoms, and this had been brought about by placebo surgery.

It is well accepted that one's aim in treatment is directed to the whole patient and to the relief of symptoms, in addition to the treatment of diseases which can reasonably be called to account for the symptoms. The use of remedies which act in a placebo fashion to relieve symptoms, either when disease is present or when it is absent, is accepted and orthodox practice, and they are frequently effective in the medically sophisticated. Failure to provide placebo solace to patients with persisting symptoms due to irremediable disease may amount to devastatingly poor medical care. It is a pity that scant scientific attention has been paid to the factors involved in placebo success—not only what causes placebo reactors to react, and conversely why some placebos fail while others succeed in the same patient, but also what factors involved in the doctor-patient relationship are important.

If placebos are orthodox and have a definite place in medical treatment, is there any justification for placebo surgery, especially if a surgical procedure entails no risk? Whilst few would recommend this avenue of approach, there are few who can deny, for example, that some patients can be separated from their abdominal symptoms by the removal of a normal appendix when medical measures have failed. No follow-up studies are available to reveal what proportion of such patients are permanently relieved. Surgery offers a much better potential as a placebo measure than anything a physician can offer: operations seem to be awe-inspiring, and there is drama with family repercussions, complete submission of the patient, possibly absolution under anaesthesia and usually a more liberal fiscal interchange. There is more than cynicism in the old adage: "If all remedies fail, prescribe an operation."

A more serious aspect of surgical practice is exemplified by those patients who are seen with identical symptoms recurring after a surgical operation at which a diseased organ was removed. The surgeon's record appears clear; the patient had symptoms, the organ was diseased, and the symptoms were relieved by the surgical procedure, perhaps with a satisfactory one year follow-up. Within this framework, the only scientific conclusion to be reached is that the surgeon successfully removed a diseased organ and prevented complications. Whether the surgeon successfully treated the patient depends on a longer follow-up. The therapeutic trial in diagnosis is not always a scientific method. In the case of myocardial ischaemia, the disease was relentless and progressive, and the placebo value of internal mammary artery ligation was easily displayed. One wonders how many established operations for more benign conditions

¹ *Circulation*, 1958, 18: 712.

² *New Engl. J. Med.*, 1959, 260: 1115 (May 28).

in which surgical indications depend on the symptoms will be scrutinized in the future. It remains a philosophical point to decide: if removal of a nuciform sac permanently cures some patients of their symptoms, when is the placebo operation justified?

Current Comment.

ANOMALOUS RIGHT SUBCLAVIAN ARTERY.

THE anomalous origin of the right subclavian artery is a condition which receives mention in few textbooks and of whose very existence many of us are unaware. Yet it is stated to be not uncommon, its incidence having been reported as varying from 0.4% to 2.0% in different series of autopsies in which the condition has been studied. The anomaly consists of the artery originating as the last vessel on the left of the aortic arch, from which point it crosses over from left to right, usually passing behind the oesophagus and trachea. The condition has received little attention for the simple reason that in a large proportion of cases it is asymptomatic, or the symptoms to which it gives rise are not severe, or their significance is not realized. It is in fact only recently that the condition has been recognized during life with any frequency. In a paper in which its radiological diagnosis is discussed, Benjamin Felson and his colleagues¹ state that "anatomists have been familiar with this condition for two centuries, yet few clinicians are aware of its existence". These authors give an adequate account of the condition and present their findings in a series of nine cases encountered in their own practice; none of these patients had any symptoms referable to the condition, and it was apparently discovered incidentally in the course of X-ray examination of the gastro-intestinal tract for other reasons. (Curiously, since other authors have not noted any unusual sex incidence, all their nine patients were females.) However, an anomalous right subclavian artery may sometimes cause dysphagia, which is in some cases severe, and is one of the causes of dysphagia lusoria, a term coined by Bayford to describe this condition in 1787. It is sometimes associated with other anomalies of the heart and great vessels, and the development of cardiac surgery in recent years has given added significance to this anomaly, which may be an incidental finding at operations on the heart and possibly a source of embarrassment.

This view of the anomalous right subclavian artery as an abnormality which is, in the great majority of cases, of no practical importance is sharply challenged in a recent article by S. Marland² and his colleagues in Paris. These authors discuss a series of eight cases encountered in the course of one year in general paediatric practice. Their attention was first drawn to the condition by the case of a six-year-old child who was investigated for retardation of growth and a basal systolic murmur. This murmur was loudest below the right clavicle, but was also heard in the right axilla and at the back. Radiological examination showed a posterior notch in the oesophagus at the level of the third dorsal vertebra, and the existence of an anomalous right subclavian artery was proved at operation. A fortnight later a second child was seen with an identical murmur, and she too had radiological evidence of an abnormal right subclavian artery. They then noted all children encountered who had a basal systolic murmur of this type, and collected 38 in one year. Of these, seven were shown radiologically to have an anomalous right subclavian artery; nine others were investigated by passing a retrograde arterial catheter, and one was found to have an anomalous right subclavian artery

which could not be demonstrated radiologically. Of these eight patients, three had sought consultation for failure to gain weight, two on account of being under weight and having a cardiac murmur (the murmur in these two cases had been labelled by a cardiologist as "inorganic"), and in three the murmur was discovered incidentally. None gave a history of dysphagia or of dyspnoea on effort. However, Marland and his colleagues are insistent that the history is deceptive. These children were poor eaters, but the parents failed to recognize signs which their children had always shown, or had slowly acquired, and the children did not complain of a difficulty in swallowing which they had always known. However, the points that were emphasized in the history were: (i) these children showed behaviour difficulties: they were emotional, cried easily, and were irritable, especially at meal times; and (ii) they all tired easily. In the event, five of these children were subjected to thoracotomy, and the aberrant artery was divided. This bold course appears to have been justified by the result, for Marland and his colleagues note a striking improvement in the behaviour and well-being of their patients after operation; appetite improved, weight gain occurred in three out of four cases, and easy fatigability rapidly disappeared. Marland and his colleagues conclude that surgical intervention is worthwhile whenever functional symptoms are present. An interesting incidental finding was the evidence that the murmur originates from the inferior vena cava at the point where it is crossed by the anomalous vessel. Another point of interest is the suggestion that basal systolic murmurs of this type are likely to indicate some anomaly of the great vessels; eight of the children in Marland's series who did not have an anomalous right subclavian artery were shown to have an anomaly of the brachio-cephalic trunk. Marland and his colleagues found evidence of a familial incidence of the condition; the 16 vascular anomalies detected were distributed among twelve families, in four of which other congenital malformations were also noted.

The surgical attack on the anomalous vessel is of course not new. A case was described by R. E. Cross in 1946,³ in which he divided an anomalous right subclavian artery in an infant, aged four months, who had serious difficulty in feeding, with complete relief of the symptoms. Other cases have since been described, but in patients in whom the anomaly was causing obvious difficulties. It appears from Marland's paper that we should also consider the possibility of an anomalous right subclavian artery in cases of failure to thrive which cannot be otherwise explained.

PROGRESS IN MALARIA ERADICATION.

In 1955 the World Health Organization adopted the bold policy of malaria eradication and, despite a certain amount of cynicism, has pressed on with it. In some areas there are obviously enormous difficulties to be overcome; they could prove insuperable, and they will certainly take time. However, in other areas, large enough to be significant in the world picture, complete success may be hoped for within a reasonable period, and the latest reports are most encouraging.

According to advice recently received from WHO, eleven countries previously affected have now eradicated malaria. Many others have almost achieved eradication or are well on the way to do so. The Americas report the most rapid progress, while even in tropical Africa, spraying with insecticides, together with the mass administration of anti-malarial drugs, is expected to lead to eradication. The details are interesting. In the Americas, eradication of malaria has been completed in the U.S.A., Chile, Martinique, Barbados and Puerto Rico. The threshold of successful eradication has been reached in Argentina, Venezuela, French Guiana, a large area of British Guiana, Guadeloupe and Panama. Eradication activities

¹ *Radiology*, 1950, 54: 340 (March).

² *Press méd.*, 1959, 67: 1083 (May 27).

³ *Ann. Surg.*, 1946, 124: 532 (September).

are in full swing in Mexico, Brazil and all the other countries of the Americas with the exception of Cuba. In Europe, eradication has been achieved in Corsica, Italy, the Netherlands, the Ukraine, Byelorussia and most of the remaining territory of the U.S.S.R. It is about to be achieved in Roumania and, with one or two exceptions, is progressing rapidly in all other malarious countries in the European Region of WHO. In the Eastern Mediterranean Region, malaria has disappeared from Cyprus and is about to disappear from Israel. Nearly all the countries in this region have launched malaria eradication programmes, and many of them are far advanced. In the South-East Asia Region, malaria eradication is progressing satisfactorily in Afghanistan, Burma, Ceylon and Thailand. Since 1958, India has been energetically carrying out a gigantic eradication programme. Indonesia has embarked on an eradication programme which will protect not only the population on the large islands but also those living on over 3000 smaller islands. Pakistan has recently announced its desire to start a nation-wide eradication campaign. In the Western Pacific Region, eradication is well advanced in Taiwan and is proceeding in the Philippines, in Cambodia and in several territories of North Borneo, while plans have been approved in Laos and Viet Nam. Pilot projects have been launched in Malaya and in Netherlands New Guinea. The report does not mention Papua-New Guinea. In Africa, eradication through the use of residual insecticides is being pursued throughout the southern part of the continent with promising results. As concerns tropical Africa, there is a growing conviction among malariologists that the attack on the mosquito with insecticides will need to be combined with an attack on the parasite transmitted by the mosquito. This would imply the massive use of anti-malarial drugs.

BITES AND STINGS.

The busy practitioner looks to the summer months to alleviate the burden of infectious illnesses, but the holiday season brings hazards of its own. Along with asthma and road accidents, this season of the year brings its quota of alarms, and even occasional fatalities, due to bites and stings of various sorts. It is therefore topical to consider a recent paper by H. M. Parrish,¹ in which he makes a survey of all deaths from bites and stings of venomous animals recorded in the United States during the five-year period from 1949-1954. In these five years 215 such deaths were reported, but the breakdown of this figure is a little surprising. Snake-bite accounted for just one-third (71) of these deaths; the greatest number followed stings by hymenoptera (bees, wasps, etc.); 39 were the result of spider bites, and 19 were due to miscellaneous causes (scorpion stings, jellyfish, etc.). There are some important differences among these groups. Death due to snake-bite generally occurs some hours after the attack; in Parrish's series, in only three of the 71 cases did death occur within an hour of the victim's being bitten. In cases of spider bite the interval before death is even longer, death having occurred in the first 12 hours in only three instances. In both these groups a large proportion of the fatalities occurred in young people, and death was due in nearly all cases to the direct effects of the venom injected. On the other hand, deaths caused by insect stings in a large majority of cases concerned persons more than 20 years of age, and death generally took place within an hour. The reason for this is that death resulting from an insect sting is generally due to anaphylaxis, and only in exceptional cases of severe, multiple stings is the toxicity of the poison dangerous in itself. The different age incidence of this group of fatalities is apparently a reflection of the age at which insect allergy develops. Australian conditions are not of course strictly comparable, but the differences are mainly in detail. In North America fatal snake-bite is most commonly inflicted by rattlesnakes;

In Australia we have the taipan, tiger snakes, brown snake and death adder. In North America the black widow spider (*Latrodectus mactans*) accounts for nearly all fatal cases of arachnidism; in Australia the related red-back spider (*Latrodectus hasseltii*) shares the honours, at least in the Sydney area, with the funnel-web spider (*Atrax robustus*). Australian wasps are perhaps less aggressive than the hornets and wasps of the genus *Vespa* of the north temperate zone; however, in the North America series, 52 of the 89 fatalities from insect stings were caused by bees, presumably in most cases honey bees, whose temperament is likely to be much the same the world over. Reference to Australian conditions would be incomplete without mention of the tick, *Ixodes holocyclus*, and poisonous marine animals. This tick is common along parts of our eastern seaboard, and is well known because of its danger to dogs, cats and other animals in these areas; its danger to man was fully discussed by D. G. Hamilton in 1940,² and from this account it appears that it is dangerous only if left undisturbed (e.g., in the scalp) for a number of days. Stinging jellyfish and other marine dangers are a separate subject and will not be discussed here.

NEUROLOGICAL SEQUELÆ OF POLIOMYELITIS IMMUNIZATION.

When Salk vaccine was introduced it was hailed for its freedom from harmful effects. Then queries about adverse reactions began to appear. G. H. Pimblett³ in Britain and E. S. Mongan⁴ in U.S.A. each reported a case of transient fever plus paresis which appeared a few days after injection of the vaccine. In Europe E. Uehlinger⁵ and S. Liebe and W. Wockel⁶ have each recorded a fatal case of spreading paralysis. N. Donaldson and W. J. McLeod⁷ saw six moderately severe reactions among 17,000 Belfast children immunized; all followed the second injection. Recently C. N. Christensen⁸ has reported on the sequelæ of 184 million injections of the vaccine manufactured by Eli Lilly and Co. There were 56 immediate (allergic) and 90 delayed reactions, 37 of these being neurological; nearly all were transient.

Pimblett³ and others asked the natural question: Could the children possibly have received live poliovirus? The symptoms of six of Christensen's⁸ patients suggested poliomyelitis. But Donaldson and McLeod⁷ had the faeces of two of their six patients tested and found no living virus. The usual picture is unlike poliomyelitis and resembles that of the neurological sequelæ of other inoculations. Three years ago these were described by P. W. Robertson and B. J. Leonard,⁹ who observed a wide variety of rheumatic and other post-infection sequelæ in young recruits. Shortly before his death Robert Wartenberg¹⁰ of San Francisco completed a monograph on neuritis. In reviewing the voluminous literature of post-injection palsies, Wartenberg said that every imaginable kind of infection might be followed by nerve damage, which presented bewildering variations. Sometimes a single nerve is affected, sometimes two, sometimes several at once or in succession. In some patients sensory fibres alone are involved, in others motor fibres alone. In most of the cases the affected nerve trunk was so far from the site of injection (sometimes in a different limb) that it could not have been directly damaged by the needle. The Salk vaccine, it would appear, is not unlike other injectable materials in its capacity to harm a small number of susceptible people.

¹ Med. J. Aust., 1940, 1: 759 (June 1).

² Brit. med. J., 1958, 1: 1299 (May 31).

³ U.S. armed Forces med. J., 1958, 9: 1659 (November).

⁴ Schweiz. med. Wschr., 1957, 87: 813 (June 29).

⁵ German med. Monthly, 1959, 4: 231 (July).

⁶ Brit. med. J., 1958, 1: 1479 (June 21).

⁷ J. Amer. med. Ass., 1959, 171: 369 (October 17).

⁸ Brit. med. J., 1956, 2: 1029 (November 3).

⁹ "Neuritis. Sensory Neuritis. Neuralgia", 1958, Oxford University Press, New York: 15, 154.

¹⁰ A.M.A. Arch. intern. Med., 1959, 104: 198 (August).

Abstracts from Medical Literature.

SURGERY.

Electrical Skin Resistance after Sympathetic Surgery.

W. MONTORSI, C. GHIRINGHELLI, G. TIBERIO AND F. LAVORATO (*Presse méd.*, March 14, 1959) have used electrical skin resistance as a control test on 85 patients who underwent lumbar sympathectomy for chronic obliterative arteritis of the lower limbs, and on 18 patients subjected to dorsal sympathectomy for Raynaud's disease. The test was carried out before the surgical intervention, and at intervals of time varying from a few weeks to three and a half years afterwards. A few months after sympathectomy, the electrical skin resistance figures for the denervated limb had considerably increased, particularly in the distal zones. At three and a half years, the values were still considerably higher than those obtained before operation, although less than those found during the first few months after operation. The authors state that this behaviour of the electrical skin resistance provides final and convincing proof of the gradual resumption of sympathetic activity. They discuss the theory of anatomical regeneration of the sympathetic chain, and conclude that, on the basis of their observations, it is improbable. They put forward the alternative theory that the resumption of sympathetic activity could result from fibres innervating neighbouring regions, or from fibres traversing the spinal network.

Sialography in Children.

B. S. FREEMAN (*Surg. Gynec. Obstet.*, October, 1958) considers that sialography can be used in children to aid in the diagnosis of any questionable mass around the region of the salivary glands with little trauma, and occasionally may prevent exploratory surgery. With proper sedatives, instruments and radio-opaque materials, it has been possible to obtain good studies in children as young as 18 months of age. No general anaesthesia is used, but sound sedation and surface anaesthesia are essential. The sphincter opening is gradually dilated and a contrast material of low viscosity slowly injected. The details of the premedication, surface anaesthesia and technique are given.

Tolerance of Skin Grafts to Radiation.

R. W. CRAM, C. H. WEDER AND T. A. WATSON (*Ann. Surg.*, January, 1959) state that there is a general impression that grafted skin tolerates X irradiation poorly; and that consequently patients who have had skin grafts in the course of treatment for malignant disease may be denied the benefits of irradiation. To investigate this problem the authors gave 15 unselected patients, on whom skin grafting had been performed after radical mastectomy for carcinoma of the breast, a routine course of X irradiation in full dosage without regard to the presence of the graft within the treatment fields. In one case the graft was of full thickness,

and in the remainder a split skin graft of medium thickness had been used. In all grafts the irradiated area showed the same skin reaction as adjacent normal skin. Generally, an erythema appeared in two or three weeks and remained for a further three or four weeks; in three patients the erythema proceeded to a mild moist reaction; this was seen both in the graft and in the adjacent skin. In no case was necrosis found after treatment, either early or late, the longest follow-up intervals being 52 and 48 months. It was found that the grafts usually remained adherent to the chest wall for a varying period up to six or eight months, and then generally became quite pliable and as mobile as any untreated graft. The late expected minor atrophic changes of radiation therapy were seen in the graft, and were parallel to those in the adjacent skin.

Biopsy of the Apex of the Axilla.

C. D. HAAGENSEN AND S. J. OBEID (*Ann. Surg.*, February, 1959), in an attempt to select those patients whose carcinoma of the breast could not be removed by the classical Halstead radical mastectomy, have performed a biopsy of the peripheral lymph node filter at several points. They tested and finally abandoned supraclavicular biopsy because they found that the absence of metastases in that area did not preclude their presence in the nearby subclavicular nodes at the apex of the axilla, and that metastasis in this latter region meant incurability by radical mastectomy. They have developed a technique of biopsy of the apex of the axilla, and have established its value in the selection of patients. Their indications for its performance, based on their experience in the first 100 cases in which it was performed, are as follows: (i) clinically involved axillary nodes, or (ii) a primary carcinoma measuring 5 cm. or more in diameter, or (iii) at least one of the grave signs of locally advanced carcinoma of the breast, i.e. oedema of the skin, ulceration (excluding Paget's disease of the nipple) and solid fixation of the tumour to the chest wall. Their triple biopsy, designed to guide them in the selection of patients for radical mastectomy, and performed as a preliminary operative procedure, consists at present of the three following steps: (i) biopsy of the primary tumour to establish the presence of carcinoma; (ii) biopsy of the tissues in the first, second and third intercostal spaces along the internal mammary lymphatic route; (iii) biopsy of the tissues at the apex of the axilla along the axillary-supraclavicular lymphatic route.

Isolation-Perfusion Techniques in the Treatment of Cancer.

O. CREECH, JR., *et alii* (*Ann. Surg.*, May, 1959) discuss their experiences with isolation-perfusion techniques in the treatment of cancer. They state that chemotherapeutic agents have failed to cure or to produce sustained palliation of most malignant lesions. This has been due to lack of truly specific cancericidal agents and also to the fact that available drugs are toxic to rapidly growing normal tissues when administered in effective amounts. Two solutions remain: a search for better agents which will produce

greater specificity and less toxicity, and a method of administering an agent to the lesion in highly effective amounts without causing toxic effects in other tissues. The authors' report deals with the method of isolation-perfusion in 73 patients. If a malignant lesion is confined regionally the treatment need be directed only to the regional environment of the neoplasm. The isolation-perfusion technique consists in excluding the tumour-bearing area from the systemic circulation and perfusing it with the chemotherapeutic agent. Such isolation can be achieved in the limbs and in the lungs, and the breast and pelvis can be treated in this way too, although complete isolation is not possible. The techniques used for the lower extremity, the upper extremity, the lungs, pelvis, breast and the whole body are described. The authors have used nitrogen mustard, PAM, actinomycin D, thiopeta (TSPA) and 5-fluorouracil (5-FU) and discuss the recommended dosage of each. They have treated 37 patients with carcinoma, 18 with sarcoma and 18 with melanoma. Among these 73 patients, 56 were treated for palliation of far-advanced malignant conditions and 17 were perfused in conjunction with the extirpation of primary lesions. Of the 60 surviving patients, in 22 the lesion appears to be controlled, in eight the disease is quiescent, and in 30 it is recurrent.

Intraaortic Nitrogen Mustard Therapy.

R. L. BYRON *et alii* (*Surgery*, April, 1959) discuss 34 patients with advanced malignant disease of the pelvis who were treated with intraaortic administration of bis (2-chloroethyl) methylamine (HN₂) in doses ranging from 0.2 to 1.6 mg. per kilogram of body weight. Of these, 31 were subjected to an exploratory laparotomy and intraaortic administration of the drug with venous occlusion at the time of operation. The remaining three patients were treated by administration of the drug through an indwelling intraaortic catheter. Seven patients showed objective improvement. There were three post-operative deaths. The authors consider that in their hands intraarterial HN₂ therapy has proved to be of some value in the palliation of advanced pelvic malignant disease. They therefore consider that patients who have malignant tumours localized to the pelvis which are not amenable to surgery or irradiation are suitable for intraaortic nitrogen mustard therapy, especially when the tumour has involved the lateral pelvic walls. The decision to use chemotherapy must usually be made at the operating table during the exploratory laparotomy. Nitrogen mustard can be administered safely via the aorta in doses of 0.25 to 1.3 mg. per kilogram of body weight.

Massively Bleeding Duodenal Ulcer.

B. GARDNER AND I. BARONOFFSKY (*Surgery*, March, 1959) analyse the case records of 235 patients with massively bleeding duodenal ulcers admitted to the wards of the Mount Sinai Hospital of New York from 1947 to 1957. They divide the patients into four groups on the basis of the amount of blood used in order to stabilize the patient. The fifth group was made up of patients who continued to bleed while on medical

therapy, or who were rushed to the operating room for emergency surgery. The mortality among 188 medically treated patients was 3.7%, whereas that among 47 surgically treated patients was 6.4%. The mortality among an additional 47 surgically treated patients who bled after discharge from hospital or were operated on electively was also 6.4%. The mortality among patients treated surgically during active bleeding was 20.8%, as opposed to 1.4% of those who underwent purely elective operations. The mortality among patients treated medically who required over two litres of blood for stabilization was 12%, whereas the mortality among similar patients treated surgically was 8.3%. Follow-up of 104 medically treated patients revealed an incidence of recurrent bleeding of 51% as opposed to 18.6% for all surgically treated patients. As far as surgical treatment was concerned, the lowest incidence (8%) of recurrent bleeding occurred after Billroth II subtotal gastric resection plus vagotomy. Review of the X-ray findings on these patients showed a higher incidence of crater ulcers in the groups with more severe bleeding. Follow-up of patients treated medically revealed that when no crater was demonstrated the incidence of recurrent bleeding was 40%, whereas when a crater was demonstrated during the patient's stay in hospital, the incidence was 72.5%. There was also an incidence of subsequent surgery of 26.7% if no crater was demonstrated and 60% if a crater was demonstrated. The authors suggest that patients who have had acute massive hemorrhages of duodenal ulcer origin should be operated upon much sooner when a crater is demonstrated radiologically.

Intralobar Sequestration of Lung Associated with Foregut Diverticulum.

J. B. DAS, O. G. DODGE AND A. W. FAWCETT (*Brit. J. Surg.*, May, 1959) describe a case of intralobar sequestration of lung, associated with a foregut diverticulum (oesophago-bronchial fistula) and an aberrant artery, in a man 31 years of age in whom a pre-operative diagnosis of bronchiectasis of the left lower lobe had been made. The specimen was removed, the oesophageal diverticulum being resected above the diaphragmatic cupola, although its origin was from the infra-diaphragmatic part of the oesophagus. There was no evidence of any diaphragmatic defect. The authors list previously reported cases, three of intralobar sequestration with foregut diverticulum and four of accessory lobe with foregut diverticulum. The embryological development of the respiratory tree is discussed and some theories of origin of this anomaly are mentioned. It is thought that the malformation is probably a variety of duplication of the foregut.

Prophylactic Castration in Carcinoma of the Breast.

M. F. ROSENBERG AND E. M. UHLMANN (*Arch. Surg.*, March, 1959) present a report concerning 200 women below the age of 50, who had been referred to them after radical mastectomy between 1942 and 1951 and who were followed up for a

period of at least five years. Seventy-eight of these women underwent prophylactic castration, either by bilateral oophorectomy or by irradiation of the ovaries shortly after radical mastectomy and before clinical evidence of distant metastases was present. Of these, 59% survived more than five years, compared with 36% of 122 patients who were not castrated. The authors note that the castration effect was especially favourable in the age group over 40 years, in which a survival rate of 69% seems to indicate that castration is of importance during early menopause. Among 66 women who died at a known date within five years after mastectomy, survival of those castrated was longer than that of the women who had functioning ovaries. The authors believe that these observations form sufficient justification for advocacy of prophylactic castration in all women with carcinoma of the breast who either are still menstruating regularly or otherwise exhibit signs of ovarian activity.

Surgical Correction of Varicocele.

H. W. SCHOENBERG AND J. J. MURPHY (*Surg. Gynec. Obstet.*, September, 1959) describe the technique of an operative procedure to cure varicocele. They believe the indication for the surgical treatment of varicocele is extreme size sufficient to produce annoying symptoms. The classical operation, that of ligation of the pampiniform plexus of veins, has proved unsatisfactory in the hands of most surgeons. Dissection of the thin-walled venous plexus is technically difficult, complications are frequent, and hematoma formation is frequently accompanied by infection, hydrocele, recurrence of varicocele and testicular atrophy. Dean Lewis, in 1906, described an operation which consisted of ligating the internal spermatic vein and the spermatic artery high up in the inguinal canal. In 1955, Robb described a modification of this procedure, and this method has been used by the authors for the past four years with consistent success. The approach is by a transverse incision at the level of the anterior superior iliac spine and the peritoneum is reflected after the muscles have been cut through in the line of their fibres. A scrotal support is worn for two weeks, during which time the varicocele undergoes thrombosis and contraction.

Splenic Pulp Manometry.

W. F. PANKE, L. M. ROUSSELOT AND A. H. MORENO (*Surg. Gynec. Obstet.*, September, 1959) discuss the use of splenic pulp manometry as an emergency test in the differential diagnosis of acute gastro-intestinal bleeding. They state that the decision as to the actual site of hemorrhage in upper gastro-intestinal bleeding can be quite a problem. (Esophago-gastric varices are the lesions responsible for such bleeding in 20% to 25% of these patients. The determination of the presence or absence of varices may be difficult during active bleeding. (Esophagoscopy, barium contrast X-ray examination, trial balloon tamponade and liver function tests have been advocated and used as aids in diagnosis. The authors use a method of combined percutaneous splenic pulp manometry and portography,

as both an emergency and an elective method in determining the presence or absence of esophago-gastric varices. Splenic pulp manometry by itself has been most useful. An 18 gauge spinal needle is introduced into the spleen and connected to a water manometer with a short length of rubber or plastic tubing. An average is taken of three sequential readings, after correction for the anatomic site of the spleen in relation to the table top. The mean pressure in patients with bleeding from varices was 143 millimetres of water, and the mean pressure in patients with bleeding from other sites in the upper part of the gastro-intestinal canal was 175 mm. of water. This procedure was used in 113 patients and proved to be 90% accurate in determining the presence or absence of varices.

Retrosternal Artificial Oesophagus.

B. A. PETROV (*Brit. J. Surg.*, March, 1959) states that it is 52 years since the first successful creation of a subcutaneous artificial oesophagus from a jejunal loop. In 1907 Herzen of Moscow was the first surgeon to complete such an operation. To prevent necrosis of the jejunal loop, the author has introduced an amending procedure. The caecum and the root of the mesentery are mobilized in such a way as to permit the jejunal loop to be transferred without risk to its vitality 10 to 20 cm. higher than is possible by ligation of the mesenteric vessels alone. The author and his associates have performed this operation more than 150 times since 1949. The advantages and disadvantages of the subcutaneous and retrosternal routes in the creation of an artificial oesophagus for benign stricture are discussed. The experience of the author has shown that the retrosternal oesophagus has considerable advantage over other ways of creating an artificial oesophagus. There is still a slight risk of viability of the transposed jejunal loop. Because of this the author has used, more recently, the colon after adequate sterilization, thereby reducing the overall risks of the operation.

Paget's Disease of the Breast.

J. K. MCGREGOR AND D. D. MCGREGOR (*Surgery*, April, 1959) point out that Paget's disease is an uncommon form of breast cancer that generally arises in the main excretory ducts of the breast and extends to involve the skin of the nipple and areola. The skin lesion is of low-grade malignancy. They state that frequently there is an eczematoid change in the nipple or areola and that this lesion may precede an obvious cancer by many years, so that it may be ignored or treated as a benign lesion before the diagnosis is established. The features of 21 cases of Paget's disease of the breast encountered in a general hospital over a 20-year period are discussed. It is pointed out that the treatment of Paget's disease of the breast is the treatment of the underlying cancer, which should be treated as radically as any other cancer of the breast. The possibility of the presence of an underlying cancer must be suspected in any case of unilateral eczema of the nipple which does not respond rapidly to local therapy, and it must be ruled out by biopsy examination.

Congresses.

FIFTEENTH INTERNATIONAL TUBERCULOSIS CONFERENCE.

The fifteenth International Tuberculosis Conference was held at Istanbul, Turkey, from September 11 to 19, 1959. We are indebted to Dr. Cotter Harvey, one of Australia's two accredited delegates, for the following account of the Conference.

The fifteenth International Tuberculosis Conference of the International Union Against Tuberculosis was held in the Assembly Hall of the University of Istanbul. Delegates numbered 1200 and came from 65 countries. Preliminary meetings of the executive committee and of the nine technical committees were held on September 11 and 12, and on September 14 the general council met and accepted the recommendations of the executive committee, the chief of which were as follows.

1. The World Health Organization was formally requested to accept as another top-priority target the elimination of tuberculosis throughout the world.

2. In view of the increasing work of the technical committees, Dr. Georges Canetti was appointed associate coordinator to Professor Heaf.

3. An appeal was made to all national associations to assist in the establishment of fellowships in tuberculosis by the Union; such fellowships have been established in France, Germany, Great Britain, Italy, Turkey and the U.S.A. The Netherlands offered to give two. Italy suggested that help might be given at governmental level.

4. The annual quota contributions of several countries, including Australia, were lowered.

5. The applications of Pakistan and North Vietnam for admission to the union were accepted. That of Taiwan was rejected; it refused to alter its name, and already one "Republic of China" is a member. The application of North Korea was deferred pending further information.

It was decided that the sixteenth International Tuberculosis Conference should be held in Toronto, Canada, in September, 1961, under the presidency of Dr. George Wherrett, the present executive secretary of the Canadian Tuberculosis Association. Under a new rule, Dr. Wherrett was formally inducted into the presidential chair at the closing meeting.

OCCUPATIONAL THERAPY AND COMMITTEE ON REHABILITATION.

The Committee on Occupational Therapy and Rehabilitation¹ met on September 12, at the Sanatorium Heybeliada, situated on the island of that name, about two square miles in area, hilly and pine-covered. It lies about ten miles down the Sea of Marmara. The rehabilitation centre is located in a sheltered valley abutting on a beach, and there the committee saw male patients engaged in learning trades, such as watch-repairing, leather work and typing.

Dr. Kervran (France) was appointed chairman of the meeting, which began its business by enlarging the committee. Representatives will be sought from Russia, Brazil, Belgium, Czechoslovakia and possibly Germany or Italy. Dr. Kervran was elected chairman for the years 1960-1962 inclusive. There was some comment on new elements recently introduced into rehabilitation (general education, functional and psychological education, gymnastics) and on the problems of settlements and the employment of ex-patients. The importance of precision in tests for cure in relation to occupation was emphasized. It is hoped that the committee will within the next three years evolve standard tests relating to (i) manual workers, (ii) intellectual workers and (iii) employees in public services. With regard to the problem of marriage of tuberculous patients, it was suggested that the economic situation took precedence over the state of the patient's health, and it was decided to make the matter the subject of a questionnaire.

It was agreed that a "Manual of Tuberculosis in the World" should be prepared by the combined efforts of all the technical committees. All countries would be asked to prepare, approximately every seven or eight years, reports on their rehabilitation position. The Australian representative¹ offered a report on the rehabilitation of the tuberculous in Australia that he had prepared; it was agreed that this was exactly what the committee desired.

¹Dr. Cotter Harvey is a member of this committee.

Finally the question of possible interchange between countries of members of the committee, of specialist doctors and of patients in the process of rehabilitation was discussed, and it was decided that, in spite of the difficulties involved in such arrangements, the project was one with which the World Health Organization might be able to assist.

SCIENTIFIC PROCEEDINGS.

This Conference differed from its predecessors in two important respects: (i) The subjects were all discussed in the form of symposia, with a chairman and a large panel of 12 to 20 participants. (ii) Ten subjects were discussed, whereas previously only three were presented (in a series of read papers). For the first time, there were non-medical subjects.

The acoustics were not good, and it was necessary to wear headphones continually. The languages were English and French, translation of the latter being hardly adequate at times. There was also a "station" in Turkish.

Symposium I: Chemoprophylaxis of Tuberculosis.

The first symposium was held under the chairmanship of Professor Robert Debré, of France.

"Chemoprotection", a word which owes its origin to the action of isoniazid on the tubercle bacillus, was divided into three phases—chemoprevention, chemoprophylaxis and chemotherapy.

1. Chemoprevention is the giving of antibacterial drugs to subjects free of any tuberculous infection. This has had some success in preventing later disease in animals, but its practical use in humans is very limited—for example, in the new-born and in close family associates. In these situations, it must be integrated with B.C.G., as the vaccine initiates immunizing processes apparently necessary for effective action of the drug.

2. Chemoprophylaxis is the treatment of known reactors to tuberculin who have no overt disease. It was generally agreed that this was an increasingly important field. The drug of choice was isoniazid, given for from three to 12 months in average doses. Among the groups proposed were: (i) persons at risk, particularly children aged under two years; (ii) known recent "converters" at any age; (iii) persons who had previously had clinical disease and were found to have some chronic disease such as diabetes or rheumatoid arthritis, or who were required to take corticoid therapy. Professor Walsh McDermott favours a minimum of two years' treatment for tuberculin reactors aged under 25 years, believing that the continued suppression of infection for this period will result in natural healing more often than without therapy. The French school maintains that chemoprophylaxis with isoniazid is now "the most powerful weapon we possess against tuberculosis". A contribution of great interest came from Kenya. In a study of a group of African natives it was demonstrated clearly that very close supervision is necessary to ensure that fit persons continue to take drugs with any sort of regularity. This problem of acceptability needs careful research before mass chemoprophylaxis can be applied. It is a fallacy to assume that "tuberculosis can be controlled by distribution of pills to the population".

3. Chemotherapy, the third phase, is self-explanatory.

Symposium II: The Problem of Atypical Acid-Fast Bacilli.

Professor Daniel Jenkins (U.S.A.) led a panel of 18 members in the second symposium. Four were clinicians and the remainder laboratory personnel.

The following definitions were given initially: (i) typical *Mycobacterium tuberculosis*, var. *hominis et bovis*. (ii) atypical: any acid-fast bacillus not possessing the cultural and laboratory characteristics of the human and bovine strains.

It was agreed that attention should be directed to those with demonstrated pathogenicity to man. At the same time, a warning was issued against applying the description "saprophyte" to any of them, and it was noted that the mouse was a more reliable animal than the guinea-pig in which to prove pathogenicity.

Runyon's four groups were accepted, as follows: (i) photochromogens, in which the colony colour acquires pigment by exposure to light. These are the most frequent cause, among the "atypicals", of pulmonary disease. (ii) Scotochromogens, which change from yellow, in the dark, to red-orange, when exposed to light. Their pathogenicity is still doubtful. (iii) The non-pigmenting "Battley" type, proven pathogenic and contagious. (iv) The rapid growers, maturing in three to

five days at room temperature, about which not much is yet known. It was admitted that the present classification is inadequate.

In actual fact, the atypical bacilli are being found more often in U.S.A. than in any other country at present.

In some countries, notably Russia, the belief is held that all are mere variations of *M. tuberculosis*. Runyon, however, insists that the organisms are a distinct species, and that they may produce serious disease which is not pulmonary tuberculosis, though clinically it is indistinguishable. His views met with general acceptance. Hundreds of cases have been reported in U.S.A., wherein no other organism was the cause of disease. Their distribution is world wide, but local concentrations apparently exist.

The identification of these bacilli has been given attention in many laboratories. The following procedures were listed as the "simplest": (i) careful examination of the colonies; (ii) systematic exposure to light; (iii) the Niacin test; (iv) estimation of catalase activity; (v) pattern of drug resistance. However, many other tests were suggested, and evidently more specific methods of identification are needed.

One speaker offered the sage comment that the greatly increasing number of cultures being made now was the main reason for the finding of these atypical bacilli.

The frequency of bronchial disease from this cause was noted, as also was the fact that some bronchiectatics were wrongly labelled tuberculous on the finding of these bacilli. The French believe that patients with pneumonokontosis are more likely to be infected with atypical bacilli.

Possibly damage to the respiratory tract is a precursor of these infections.

The clinician was urged to be vigilant, especially in an infection not responding to treatment, to consider whether it might not be due to an atypical rather than the typical *Mycobacterium*.

Treatment with isoniazid in high dosage, cycloserine, rest and excisional surgery was advised.

A final warning was given by the reporting of patients with photochromogen or other mycobacterial infection who acquired superimposed tuberculosis after residence in tuberculosis hospitals or sanatoria.

Symposium III: Indications for Surgical Treatment of Pulmonary Tuberculosis.

Sir Clement Price Thomas, presiding at the third symposium, stated that the objective of any treatment was "to make the patient free of pulmonary tuberculosis". This remains a problem of the individual, and due respect must be paid to immunological responses. The speakers who followed ranged widely over the subject, offering experiences in both developed and under-developed countries.²

Despite the chairman's well-known predilection, it was generally agreed that resection was the operation of choice, and that only exceptionally should collapse therapy be brought into use. Prolonged chemotherapy now meant that major surgery could be avoided in the great majority of cases, but that the indications for and the exact timing of surgical intervention were now becoming more clearly cut.

A surprising follow-up investigation was offered from Great Britain of 187 patients deemed suitable for thoracoplasty, who for various reasons had not undergone operation. After a period of from three to 12 years, 67% showed radiological improvement, and only 10% were worse. Thirty-six patients had relapsed, but half of these had refused treatment of any sort. By the end of 1958, only four still had "positive" sputum. It was suggested these figures compared favourably with many surgical follow-up investigations. However, Dutch figures on 637 patients, five or more years after resection, showed 58 (9.2%) deaths, of which 16 were "operative". Of the remaining 42 patients, only 14 had died of tuberculosis. Of the survivors, 98% had sputum conversion, and 94% "were again leading a full active life".

The Russians demonstrated a new instrument, "UKL-60", designed for rapid suturing of the lung root with tantalum clips. It was held to be simple and speedy to use, and fistulas were said not to result, nor were foreign body reactions noted.

The problem of the "open negative" cavity was discussed but not solved. However, the following standard main indications were accepted: (i) persistent cavitation: (ii)

mechanically unfavourable conditions, such as atelectasis and extensive localized fibrosis, with bronchiectasis; (iii) the presence of tuberculomas; (iv) localized lesions in the presence of drug resistance.

Finally, note was made of the difficulties attending surgery in under-developed countries, in terms of adequate chemotherapy, education of patients and public, economics, and the possibility of obtaining "ideal conditions" under which to operate. It was held that given favourable factors, results in those countries might be expected to approach those in the more favoured ones.

Symposium IV: New Anti-Bacterial Drugs.

This subject was given an airing for three hours under the chairmanship of Professor Hellmeyer (Germany), but no real challenge emerged to the favoured three—isoniazid, streptomycin and P.A.S. in various combinations.

Cycloserine has been proved to be an active drug, though in the optimal daily dose of one gramme, central nervous system toxicity is observed in 5% to 10% of cases. Its efficacy is enhanced by combination with isoniazid, and this pairing is deemed "very useful under special circumstances".

Pyrazinamide still causes concern by reason of its hepatotoxicity. It should never be given to ambulant patients, and liver function tests must be employed regularly to give warning. Reduction of the daily dose from three to one and a half grammes suggests diminution in the incidence, though curiously not in the severity when it occurs, of liver toxicity.

Kanamycin was extolled by the Japanese, who received some support from the Italians. Their claim that it is "almost comparable to streptomycin" awaits confirmation.

A great deal of laboratory and clinical research has taken place in France with their new alpha-ethyl thioisonicotinamide (1314Th). Its mode of action resembles that of isoniazid but it is "five times less toxic". It is not a derivative of the latter, and crossed sensitivity does not occur. However, it is badly tolerated, and cessation of its use was required in up to 40% of patients. This drug is certainly still in the experimental stage.

From Ireland and Russia came evidence of attempts to find improved antimicrobial agents, especially those derived from isoniazid, but little success has yet attended their efforts.

The Edinburgh school summed up the choice of the newer drugs as follows: (i) An effective technique for tests of efficacy is by serial counts of viable tubercle bacilli in the sputum, especially those resistant to the three standard drugs. Effective drugs cause a fall in the count, which may be succeeded by a rise if resistance develops to the new drug. (ii) By this technique cycloserine has a weak effect, while pyrazinamide and 1314 are relatively powerful. (iii) Tetracycline (2 grammes twice a day) is relatively effective in preventing resistance to viomycin and perhaps cycloserine, but ineffective to pyrazinamide and 1314. (iv) For patients whose bacilli are resistant to the standard drugs, viomycin (2 grammes twice a week) plus tetracycline (2 grammes twice a day) are a practical, but relatively weak, combination. Cycloserine plus pyrazinamide, and perhaps 1314 plus pyrazinamide, are probably more powerful, but more toxic combinations.

Symposium V: Relapse of Pulmonary Tuberculosis after Treatment.

Medical Treatment.

Professor Bariety (France) led this discussion. Care was taken initially to ensure that exacerbation of latent disease was not confused with true relapse—namely, bacterial conversion or radiological worsening after evident inactivity (by both criteria) for two months or more. Some two-thirds of relapses occur in the first two years, but an appreciable number, up to 25%, between three and five years. Its incidence depends on many factors, such as the nature and extent of the disease at the time of diagnosis, the patient's general condition, economic status and cooperation, and the type and duration of chemotherapy. Drug resistance did not appear important as a cause, though of course the prognosis was considerably worse if the patient's bacilli were found to be resistant at the moment of relapse.

It was recognized that there are two influences tending to increase relapse rates: (i) the great increase in the number of sputum examinations carried out nowadays; (ii) the continued survival of patients with far advanced disease who would have died in the prechemotherapy period.

The most important single cause has been too short a duration of chemotherapy. The Edinburgh figures show a

²The proceedings of the Conference have been published in two volumes.

relapse rate of 14% after under six months' treatment, 7% after six to 12 months' treatment, and 0.8% after 12 to 18 months' treatment; only one in 260 relapsed after more than 18 months' therapy. Of 29 patients with persistent cavitation ("open negative cavity"), 25 were well 18 months or more later, while four had relapsed. Resection for new patients thoroughly treated by drugs may now be obsolescent.

Again the under-developed countries had an important contribution to offer. In stressing that the best available treatment must always be employed, it was pointed out that the word "available" had a different meaning to them. For instance, economics, accessibility and the like may limit availability (at the top level) to 10% or less of the affected population. Under such circumstances, the use of isoniazid alone may be justifiable, while pneumoperitoneum has the additional merit of keeping the patient under constant observation. Failure of a patient to cooperate may be an indication for surgery by resection.

The site of relapse came under discussion, with a suggestion that relapse in an area of old disease indicated that there had really been continual activity in that site.

Several contributors found that chemotherapy of ambulant patients did not increase relapse rates, while there was one speaker who propounded the theory that indefinitely prolonged chemotherapy was the best means of avoiding relapse.

Surgical Treatment.

This well-organized symposium under Dr. Roger Mitchell (U.S.A.) followed fairly closely along the lines of the previous one.

Again it was emphasized that reactivation was not the same as relapse, and further, that many relapses after surgery were really "medical". Inactivity was defined here as "static X-ray, negative sputum and no cavity for six months". Relapse was defined as "positive bacteriology and/or X-ray worsening after inactivity, after surgery". By definition, then, the patient with an "open" lesion cannot relapse.

Figures from the U.S. Veterans indicate a slightly higher relapse rate in patients medically treated than in those having surgery in addition, and more severe and earlier relapses after thoracoplasty than after resection.

Most surgical relapses occur in the first year, but with improving chemotherapy, they are becoming less frequent and less severe. Unfavourable factors are bronchial disease, contralateral disease, "positive" sputum, drug resistance, poor pulmonary function, other complicating disease and inadequate chemotherapy. Probably surgery is not needed for the "open negative" case. It is now required largely for chemotherapy failures.

It was agreed by both sections that the problem of relapse could be practically solved if the patient was healed "in time and adequately". However, the present high incidence emphasizes the need for education both of physicians and of the general public regarding the factors influencing relapses in pulmonary tuberculosis and the means of preventing them.

Symposium VI: Health Education in the Light of the New Methods of Prevention and Treatment of Tuberculosis.

New ground for the International Union Against Tuberculosis was broken by this and the following session, wherein non-medical workers made important contributions. Dr. Lokce (Turkey), Secretary-General of the Organizing Committee of the Conference, was chairman, and the subject with its many ramifications was thoroughly thrashed out. At the outset it was emphasized that education is more important now than ever before, if eradication is to be the goal. Better planning is needed, the scope must be widened, and volunteer help will be most valuable, especially in the older age and lower social groups, who have proved hard to reach. Psychological and emotional reactions need appraisal, as well as knowledge, and this applies to all groups of the community, not excluding medical personnel. One speaker was gloomy about the possibility of obtaining "right-thinking" from the Press, which consistently fails to present the proper angle, preferring sensationalism. It was agreed that intensification of health education was especially necessary in under-developed countries, though of course there could be no uniform programme suitable to them all.

The use of widespread chemoprophylaxis was not approved by the panel, and Professor Walsh McDermott (U.S.A.) came out with the statement that "neither B.C.G.

nor chemoprophylaxis will be the most important measures for control in under-developed countries. The most important is the treatment of patients with the disease: all the others are secondary". He expressed his concern over the reluctance of physicians—and the International Union—"to utilize the enormous development represented by isoniazid". "The way to reduce the incidence of pulmonary tuberculosis is to treat it, in organized fashion, with all the personnel available." Admitting that there are not enough in under-developed countries, the programme must go on, possibly with help from lay staff.

Returning to education, it was agreed there were two standpoints: (i) the patient and his family; (ii) the general public. In regard to the latter, it was wisely pointed out that the average members of the public were not keen to hear about tuberculosis; only when it struck them or their families did they become interested.

The professional health educator is an American innovation—there are 500 of these specialists in the States—and they are coordinators of teams comprising public health personnel, educationists, auxiliary field workers and socially-minded volunteers, including ex-patients. This is an ideal which, of course, cannot be achieved in under-developed countries; but it was important everywhere to find what the people believed, and what was their attitude. The message given them would vary accordingly, and for illiterate areas the value of audio-visual aids was emphasized.

In case-finding, there was general agreement with the proposition that mass X-ray surveys were necessary only in high-incidence countries; otherwise, the Mantoux-test should be the initial screen, only the reactors being radiologically examined. This principle is being increasingly followed. In Canada, "they are moving over to skin testing", though radiologically examining all aged over 40 years "for other reasons". De Abreu was there to state that radiation hazards were negligible "even if rayed three times a year for thirty years".

B.C.G. received passing mention, McDermott favouring its use in "any area small or large, where children aged fifteen have a 20% to 25% positive Mantoux rate". But B.C.G. he regards as a "minor tool", compared with treatment.

Treatment at ambulatory level was accepted, though hospital was advised for patients on first detection (and emphatically not for "chronics"). One speaker thought that treatment should be compulsory.

From the floor of the house came three simple points in education, to conclude: (i) The patient's sputum is the key source of infection. (ii) The best means of diagnosis is by radiology. (iii) Tuberculosis is a curable disease. A fitting finish.

Symposium VII: The Role of the Public Health Nurse and the Social Worker in Tuberculosis Control.

In this session also, paramedical workers had a prominent place. The opening speaker emphasized the increasingly important role played by these two groups with the advent of techniques such as tuberculin testing and vaccination, domiciliary chemotherapy and fluorophotography, and with all that was involved in case finding.

Early in the discussion, it became evident that the special training required made it almost impossible for any one person to be both nurse and social worker. However, an attempt at defining their duties revealed considerable overlapping, and some speakers from more developed countries held that the public health nurse could carry out all the duties implied in the title, such as infant welfare work and care of the aged, in addition to tuberculosis control.

The basic tasks of the worker are as follows: (i) Maintaining of close contact with the physicians. (ii) Surveying the domiciliary environment, with special attention to the economic and social problems of the family unit. (iii) Reporting on the public health aspects as regard risks of infecting others, and arranging for the examination of all contacts. (iv) Reporting on the need for economic, nursing or other assistance in the home. (v) Maintaining follow-up control of both the patient and the family unit.

Recent developments, such as the use of B.C.G., the serial use of the tuberculin test in case finding, the increase in domiciliary chemotherapy and the importance of maintaining accurate central case registers, make it essential that the worker shall be a good public relations officer.

It was recognized that in many countries there is a great shortage of social workers, and Turkey is meeting this by setting up special training schools for the purpose, with a course of three years covering the essentials. The delegates

advocated small clinics in charge of nurses, though others were sceptical of this measure. But in many primitive countries, their establishment is obviously the only way at present to carry on the fight in rural areas.

The following conclusions were reached: (i) Nurses and social workers play an indispensable role in tuberculosis control. (ii) They are particularly important on the preventive side. (iii) They are facing expanded duties with newer measures, especially of therapy, and their responsibilities are greater. (iv) This in turn leads to the need for wider training. (v) No single pattern of social work can be acceptable to all countries.

Symposium VIII: New Methods in the Rehabilitation of the Tuberculous.

This subject was very carefully discussed under the chairmanship of Dr. Oppikofer (Switzerland), who posed a series of questions to his panel.

It was accepted that with improved modern therapy, rehabilitation has become more important than ever; for instance, many patients who would formerly have died are now able to return to some form of gainful employment.

As a brief definition, rehabilitation implies a series of measures designed to integrate the patient as completely as possible into normal life. When it is adequate, relapse is less likely; several speakers with wide experience recorded a relapse rate of only 4% among their patients who had returned to work. Those needing it, in a "complete" form, are apparently between 10% and 20% of ex-patients, the figure being governed to a considerable degree by the social and economic conditions of the individual country. In "partial" form, all patients are benefited, as rehabilitation assists in improving their psychological as well as their medical condition. It was therefore accepted by all that rehabilitation is an integral part of the general treatment plan with which it proceeds concurrently, and it is quite wrong to introduce it at the end. Some countries have rehabilitation centres associated with their sanatoria, though a few prefer to carry out rehabilitation "on the job". (Hong Kong, incidentally, has no rehabilitation problem, as practically all patients there are ambulatory and continue uninterrupted at work.)

Speakers were unanimous that the physician must remain in charge, and that he must obtain complete cooperation from the whole team, including occupational therapist, psychologist, and vocational and employment officers.

All measures which improve function are important, including physical training, on which the Russians lay great stress; this includes many kinds of sport. These should be continued after the "cure" is complete.

The old concept of a "sheltered life" for the tuberculous is outmoded, though he should ideally be taught a special skill which requires a minimum of exertion, provided that he cannot return to his former job for any reason. In this connexion, a recent law enacted in Iran is revolutionary. All employers there are compelled to re-employ their workers, at a level suited to their health. If they are unable to fulfil this obligation, they must pay the worker a sum of money equivalent to 30 months' wages. However, the healed tuberculous patient of today can do "almost anything", and if home conditions are reasonable, he should not remain in a sanatorium to complete his cure, occupying a bed unnecessarily.

Chronically infectious patients capable of productive work continue to present the most difficult problem, and maybe some type of "village settlement" is still needed for them. At the other extreme, industrial rehabilitation as carried out in the Philips Clinic, Eindhoven, said to be "the final phase of a historical development" of which the settlement was the first, would seem to be an increasingly useful measure in more developed countries.

It was emphasized that all these schemes cost money, but it is money well spent, though many countries "starve" this, the third phase of treatment. In the long run it costs more to provide a tuberculosis service without rehabilitation, because the latter not only prevents relapses and chronic invalidism, but increases productive capacity.

Finally, the need for research was recognized—for example, by having control series, by studies of capacity for work, by pilot studies in small centres in underdeveloped countries and by the compilation of statistics.

Seminar I: Acquired Immunity in Tuberculosis.

Professor R. Cruickshank, as chairman of the first seminar, in his opening remarks stressed the complexity of

the immunogenic fractions of *M. tuberculosis*, and of the whole concept of immunity in tuberculosis. He held that cellular immunity probably played a greater part than, as had been hitherto thought, humoral antibodies.

Professor Raffel pointed out that two groups of factors were involved, specific and non-specific. The former are either humoral or cellular. Humoral antibodies are probably not related to immunity, but may be of help in diagnosing active from inactive tuberculosis. At present work is being carried out on this problem. The following evidence supports this: (i) Passive transference of serum from immune to non-immune animals does not transmit resistance. (ii) The presence and quantity of antibodies cannot be correlated with resistance. (iii) During response to B.C.G., total body irradiation suppresses antibodies, but does not prevent the acquisition of resistance. With regard to cellular factors, experiments have been carried out on macrophages, but results unfortunately are controversial. Similarly, work with lymphocytes has been inconclusive.

In relation to non-specific factors, there is good evidence that a substance does circulate in the blood during the period of infection, which has a marked effect on *M. tuberculosis*. This substance has been shown to be bactericidal *in vitro*. It is an alpha globulin, but it is not an antibody.

Professor Youmans has attempted to find a substitute for living vaccine. By grinding the bacteria with powdered glass he has been able to isolate four fractions of varying immunological capacity. He posed the question whether immunity is dependent on isolated fractions, and how far this may explain the variations of resistance in different human races.

Dr. D'Arcy Hart discussed the variable results of B.C.G. vaccination in different countries. Low-grade tuberculin sensitivity in the tropics may be an indication for giving B.C.G. He also pointed out that conversion is not an accurate guide to the degree of protection given.

Dr. Wallace Fox recounted an interesting controlled experiment he had carried out in India, treating two groups of patients with severe and mainly "sputum positive" tuberculosis. Two hundred were "domiciliary", with very little rest, on a poor diet of less than 30 grammes of animal protein per day and their drug therapy was "irregular". The other 200 were treated in a sanatorium and had an intake of more than 50 grammes of protein per day. Patients in each group were given 200 mg. of isoniazid and 10 grammes of P.A.S. per day. The results were equally good in both groups. This discounts considerably the importance of nutrition and socio-economic factors in immunity.

Seminar II: The Role of B.C.G. Vaccination in the Different Countries of the World.

A distinguished board of 24 members, with Professor Frappier (Canada) as its president, sat in judgement during the greater part of the last day, on B.C.G., that more than ever controversial vaccine. The decisions they sought were: (i) What are the factors making it possible to judge its efficacy? (ii) What role does it play in different countries, and how do they investigate its efficiency?

Dr. Pollock (U.K.) opened by giving a summary of the Medical Research Council's controlled investigation, recently published in the *British Medical Journal*, on 56,000 children up to the age of 14 years who had been vaccinated in 1950-1952, and who had had no known contact with a case of tuberculosis. The follow-up results indicated a high degree of protection, both with B.C.G. and with vole vaccine.

Indian figures, however, in some 4300 vaccinated versus 5400 unvaccinated persons, showed an attack rate of 1.9 per thousand in the former against 1.4 per thousand in the latter. In this study the effect of B.C.G. was negligible, possibly because of the effect of heat or sunlight on the vaccine, and also the low-grade allergy shown by Indians, which may indicate low immunity.

French Africa prefers the oral route, as originally used by Calmette, deeming it to be just as efficacious, the vaccine being given repeatedly at monthly intervals; other French speakers supported this. Of great interest at this stage was a contribution by Professor Gernez-Rieux (France). His group had followed up no less than 5800 of the new-born infants originally given vaccine orally, in three doses, by Calmette himself in 1925. They checked all known records until these subjects reached their present age of 34 years, or had died. "About 50%" of contemporary infants had not been vaccinated, and it was found that the death rate from tuberculosis among those given B.C.G. was less than half

that of the unvaccinated, indicating protection lasting for over 30 years.

Over 11,000,000 infants in the Soviet Union are vaccinated annually, by the oral route initially, then by injection at the ages of two, seven, 12 and 15 years before going on to university or technical school. The Russians are satisfied that there is a great decrease in morbidity among these children.

Norway, one of the world's "lowest mortality" countries, has carried out a mass B.C.G. campaign since 1947. In that year, cases of military tuberculosis and meningitis amounted to 13% of all notified cases in young adults. In 1957, only one case was reported.

By contrast, Holland, with an even lower mortality rate, has never used B.C.G. on a large scale. Its mortality figure has fallen from 200 in 1932 to 12 in 1952, and to 4.3 in 1958, while there has been a decrease of new-case incidence of 55% in the past six years. Credit is given to sociological and economic factors, but especially to public health measures (before chemotherapy). This contention met with full support from U.S.A., where the vaccine has also played very little part. However, figures of decreased incidence of meningitis were accepted as undoubted evidence of the value of B.C.G. vaccination.

Dr. Heimbeck (Norway) one of the pioneers, stated that his 1930 group of vaccinated nurses were still under observation, and also that no case of pulmonary tuberculosis had occurred among nurses in Oslo in the past ten years, though they were deliberately exposed to infection. His objective, now as then, is to boost immunity by natural infection after B.C.G.

At this point chemoprophylaxis entered the discussion, and one speaker pointed out that there was no competition, as isoniazid therapy should be complementary to B.C.G. There was no possibility of giving the drug to all "negative" reactors, but it should be given to recent "converters". Vaccination was justified in high-incidence areas only, and revaccination was then desirable on the analogy of other infectious diseases. Further, a persistently positive Mantoux reaction might not indicate immunity, but spontaneous infection. (Hence the desire of some to continue isoniazid with B.C.G.)

The Turkish delegate stressed the fact that chemoprotection would be very costly, assuming that four persons would need it for every active case. B.C.G. presented a more reasonable and practical approach from a public health aspect.

Professor Walgren (Sweden), another pioneer, admitted that there was no need for B.C.G. in low-incidence countries (a significant statement, coming from one of its hitherto most enthusiastic advocates). He conceded the loss of the diagnostic value of the tuberculin test to be a powerful argument against its general use, and agreed that selective vaccination among high-risk groups, such as hospital personnel, was all that was required. He made four points: (i) The principal benefit of vaccination was the prevention of immediate consequences. (ii) It had little, if any, effect on later infection. (iii) The "immunological state" was of only limited duration. (iv) Early use of isoniazid in primary infection should reduce the morbidity rate in tuberculosis.

In summary, apart from the controlled study in India, good protection was reported from all studies, lasting in one case over 30 years. It was generally agreed that B.C.G. was not indicated in all countries, but that those economically under-developed and with known high tuberculosis incidence should benefit most. Chemoprotection could be integrated as well into control programmes.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

PHOTOGRAPHY AND MEDICAL SCIENCE.¹

[From the *Australasian Medical Gazette*, February, 1896.]

SOME few weeks ago the Australian public were startled by an announcement by cable that a method of photographing objects through opaque media was being utilised

¹From the original in the Mitchell Library, Sydney.

by the medical profession in England for the purpose of examining the interior of the human body, and some enthusiasts went so far as to assert that fractures and diseases of the bones might be diagnosed by its employment. We live in an age when the performance of apparently impossible tasks is of daily occurrence, yet we believe that such an announcement is, to say the least, premature. Possibly what is now engaging the attention of the profession is the photographing of the cavities of the body e.g. the stomach, bladder, or eye. This is however not entirely new. A couple of years ago Dr. Kollman of Leipzig, described in one of the German medical journals, a method of photographing the living urethra. Dr. Kollman so modified Oberlander's urethroscope as to enable it to carry a small camera, by means of which he obtained some very clear negatives of the mucous membrane of the urethra, both healthy and diseased. Mr. Lucien Howe of Buffalo U.S.A. in a paper read before the Ophthalmological Society of the United Kingdom, in October, 1893, described a method of photographing the interior of the eye by means of orthochromatic plates. Probably these facts have been enlarged upon, and the sensational cablegram referred to is the result.

Undoubtedly photography is a great aid to medical men. By its means we can show clearly the progress of a case, and the benefits derived from surgical operations. If photography in natural colours should ever become an accomplished fact it will be invaluable in study of skin diseases. Every large hospital throughout the Australian Colonies should possess a dark room fully equipped, and it should be the duty of the resident medical officer to obtain photographs of all interesting cases in the wards.

Correspondence.

THE CHALLENGE AHEAD.

SIR: We must all be grateful to Dr. Büttner (Med. J. Aust., January 2, 1960) for his timely exposition of the Nazi philosophy as it was explained to him. We were in danger of forgetting what a lot of pseudo-scientific boloney it all was.

Yours, etc.,

A. M. LIESHOLD.

65 Chapel Street,
St. Kilda,
Victoria.
December 30, 1959.

SIR: Dr. Everingham states that Hitler and Mussolini were "theists". He is right, if he means "devoted to Thor and Wotan and Blood and Race and earth-gods". He is wrong, if he means "God-fearing" in the Judaic-Christian sense, so that their personal piety overflowed into their politics, and "the fear of the Lord" was, for them, "the beginning of wisdom".

He questions the principle "No God, no freedom", for he fails to see that if personal rights and freedom and dignity are not a gift from God, they can come only from the State. And if the State gives freedom, the State can withhold it, or take it away, and there is no freedom. If one person has no freedom in his own right, neither have ten million, for nought multiplied is still nought. The gathering of persons together in society does not create freedom. It imposes obligations to respect the freedoms and rights of neighbours. Dr. Everingham objects that atheists fight for freedom. But they do this only by being illogical, trying to restore with the left hand what they have destroyed with the right. Since David the King described him in the Psalms (14.1 and 53.1), the atheist has not improved. Dr. Everingham then confuses Franco with Hitler and Mussolini, evidently not understanding the distinction between authoritarianism and totalitarianism or tyranny. The former admits a natural law which is a participation in the Divine Eternal Law, while the latter rejects these.

Fortunately for the world and for us, Americans appreciate these things. They devote the Fourth of July to the proclamation of man's rights and liberties, and Thanksgiving Day to the acknowledgement of their source. Their Founding Fathers wrote these things into their Declaration of Independence, asserting the rights of man, not as an assertion of man, but as the "unalienable" gift of his Creator, written in "the laws of Nature and of

Nature's God". Washington warned in his farewell address that politics is a branch of morals, and morals of religion, and he declared the first official Thanksgiving in 1789 in the words "It is the duty of all nations to acknowledge the providence of Almighty God, to obey His will" and so on. Lincoln revived Thanksgiving, urged his fellow citizens to "pray with all fervency and contrition", and made Thanksgiving a national as well as a State holiday. Tom Paine insisted that human rights are equal only because "every child born into the world must be considered as deriving its existence from God". Jefferson wrote that the only firm basis for the liberties of a nation is a "conviction in the minds of the people that their liberties are from God". And Chief Justice John Marshall, who "put the flesh on the bones of the American Constitution", wrote: "There are principles of abstract justice which the Creator of all things has impressed on the mind of His creature man, and which are admitted to regulate, in a great degree, the rights of civilized nations." And Eisenhower declared in his Philadelphia speech of August, 1955, that "our nation is ranged with those who seek attainment of human goals through a government of laws . . . rooted in moral law, reflecting a religious faith that man is created in the image of God".

Perhaps we should thank Dr. Büttner for his sympathetic account of Nazism. Actually it is superfluous, for Australians already know the beast. Useful, however, is his statement that "religious worship is free" under Nazism, for, when this is coupled with Dr. O'Day's statements about Hungary and Tibet, the community of propaganda techniques is evident.

Dr. Büttner should, however, have told us more about "miscegenation" of races, and its prevention. Surely some of the technical refinements are worthy of note—for example, that the surviving relatives witness the gas-chamber operations, and later savour the smoke from the furnaces. Ten million were accounted for in no time. Dr. Büttner describes the system as faultless.

In the challenge ahead, let us hope that Australia, in spite of the O'Days, Everinghams and Büttners, will, before it is too late, heed the lesson that was taught to the men of old, and has since been taught many times even to the present day: "Know thou, and see, that it is an evil and a bitter thing for thee, to forsake the Lord thy God." (Jeremiah 2.19.)

Yours, etc.,

225 Macquarie Street,
Sydney.
December 25, 1959.

VICTOR J. KINSELLA.

SIR: The letters of my opponents are composed mainly of ridiculous slander. Now abuse is no argument. To illustrate this, let me, as a correspondent suggests, write a medical letter.

Among physicians, surgeons and specialists are to be found a few dishonest people, and all of them, honest or dishonest, occasionally make tragic mistakes. It would be nonsensical to use this against the science of medicine and its followers who have dealt such blows to diphtheria, scarlet fever, meningitis, lobar pneumonia, streptococcal septicæmia, yaws, leprosy, tuberculosis, malaria, gonorrhæa, syphilis, cholera, typhoid, typhus, bubonic plague, diabetes and pernicious anemia, and have assured such unparalleled safety to mother and baby.

I freely admit that Communists do make mistakes, that some turn out to be villains. That is true, of course, of any body of human beings. The achievements of the Communists who have truly used Communist science are undeniably so tremendous that such faults sink into insignificance as do those of medical men. At the moment when Communism leads the world in science and education and is about to abolish war and begin interplanetary travel, it is surely time to study its science in our own interests.

The Australian medical profession is now in the main directly or indirectly a servant of the State. The old age and invalid pensioners, the returned soldiers and their families, the insurance-medical and workers—the grants to hospitals, really form the backbone of medical practice. This means heavy expense to the State, which is far from solvent and has resorted to intense taxation and inflation. Should another crisis occur as in 1929, the State would either cut social services or inflate heavily. In either case, the profession would be suddenly and severely impoverished. We may then really envy our socialist confrères, who are well paid by States that are solvent and do not inflate.

It seems obvious that what Marxist theory has to say on this subject is likely to be of vital interest to us. An objective study of it is strongly indicated.

Yours, etc.,

196 Nepean Highway,
Aspendale, Victoria.
December 21, 1959.

G. P. O'DAY.

[This correspondence is now closed.—EDITOR.]

CONSCIOUSNESS DURING SURGICAL OPERATIONS.

SIR: In a recent edition of the *British Medical Journal* (October 24, 1959), the leading article was entitled "Consciousness during Surgical Operations". Warning was given of the real possibility of patients being conscious whilst under the effect of relaxants during major surgical procedures.

This brought to my memory an example which I observed as a student several years ago. An elderly man, following a prostatectomy, told me that he remembered all that happened during his operation, and that he suffered terrible pain but was unable to do anything about it (under relaxants). No doubt he was to some extent analgesic, but it was certainly a real experience.

Perhaps this happens only very occasionally; but we ought to be aware of this distressing but avoidable possibility.

Yours, etc.,

214 Melbourne Street,
North Adelaide,
South Australia.
December 15, 1959.

A. O. ROBERTSON.

MEDICAL MATTERS AND THE PRESS.

SIR: I am a journalist and the author of an article on Parkinson's disease which appeared in the *Daily Telegraph* on October 7, this year. This article has led to some most vituperative and inaccurate correspondence in *THE MEDICAL JOURNAL OF AUSTRALIA* of the issue of November 21, 1959. It is to this correspondence that I wish to reply so that the inaccuracies may be corrected and the record set straight.

Firstly, Mr. Miller states: "It is interesting to speculate as to why the universally accepted and widely practised techniques used throughout the world during the past four years in the treatment of Parkinson's disease should continually be used in newspapers of this country for the blatantly open or thinly veiled advertisement of certain neurological teams and institutes . . ."

It is not necessary for Mr. Miller to speculate. The reason is simple—these operations have captured the imagination of the public and of writers all over the world, as they are the first successful attempt to provide relief for sufferers of this still incurable disease. Surgical methods of alleviating Parkinson's disease have been the subject of articles in the American publications *Life* and *Time*, and in a popular German illustrated weekly. Closer home, articles have appeared in the *Australasian Post*, the *Women's Weekly* (June 4, 1958), *The Sun* on July 16, 1958, and on September 18, 1958, and finally in the *Daily Telegraph* on October 7, 1959, to name but a few. Indeed, the guardian of medical ethics—the British Medical Association in Australia—chose this subject as being suitable for publicity in the lay Press.

Secondly, Mr. Dowling says: "The article is entirely uncritical, makes a Hollywood drama out of a routine procedure and, by the art of omission of facts, could lead to many misconceptions in the mind of the reader. The implication is, in effect, that there is only one operation worth doing and but one place where it can be performed . . ."

On June 4, 1958, an article appeared in the *Women's Weekly* informing the public that this operation would soon be performed at the Cerebral Surgery Research Unit at Callan Park. On June 17, 1958, an article appeared in *The Sun* describing an operation performed at Sydney Hospital and telling the public of its success in a much more dramatic fashion than did my article in the *Daily Telegraph*. Yet the surgeon who performed this operation at Sydney Hospital and who, according to Mr. Miller,

"cannot emancipate himself from the responsibility" for such an article is one of the critics whose letter appeared in your publication on November 21.

On February 6, 1959, an article appeared on page 7 of *The Sydney Morning Herald* informing the public that St. Vincent's Hospital now had an instrument which would enable surgeons at that hospital to perform this operation with a 99.9% accuracy. Yet the *Herald* reporter had not been correctly informed that this same instrument had been in use for more than nine months at another Sydney hospital whose staff had given one of the St. Vincent's surgeons all possible help with regard to the purchase and use of this instrument.

The mention of 99.9% accuracy surely suggests to the readers of this particular piece that such accuracy had not previously been achieved, or was it meant to "advertise" the fact that the operation could now be done at this hospital? If the surgeon cannot "emancipate himself from the responsibility" for such an article, can Mr. Miller and Mr. Dowling explain the need for—or justification of—such information to the public which, as Mr. Dowling points out, "by the art of omission of facts, could lead to many misconceptions in the mind of the reader".

Mr. Dowling further misinforms your readers that "chemical methods are more extensively employed in accredited centres the world over than diathermy . . ." While it is not my province to judge, it is evident from a review of the literature and reports of a symposium on this form of surgery presented at the International Congress of Neurological Sciences in Brussels in 1957¹ that diathermy coagulation is used far more extensively all over the world than chemical methods. For example, diathermy is used exclusively in Germany and Sweden, predominantly in the United Kingdom, and in the majority of centres in the United States excepting one in New York. I am reliably informed that chemical methods have been abandoned by several clinics overseas as well as in Australia.

Mr. Dowling severely criticizes the bad form of my article "In making a comparison of an unfavourable nature to that most experienced New York clinic where this surgery originated . . ." The relevant paragraph of my article reads as follows: "Their results compare more than favourably with those achieved using a similar method in New York where the mortality is three per cent, and another three per cent suffer from side effects." No mention of any particular New York clinic was made.

Further, may I as a layman refer Mr. Dowling to a paper entitled "The Globus Pallidus as a Surgical Target" by Cooper and Poloukhine (1956),² where the authors state: "An important avenue of investigation was opened by Spiegel and Wycis, who developed a stereotactic instrument for precision localisation of lesions to be made deep in the human brain." It is generally known that Spiegel and Wycis in 1947³ were the first to use stereotactic methods in human patients, and these authors in 1954,⁴ as well as Riechert in 1953,⁵ published results of their operations for the relief of Parkinson's disease several months before similar operations were begun in the New York clinic in which Mr. Dowling claims this surgery originated.

Mr. Dowling takes exception to the term "pioneer" which was used in the following context in my article: "The team are pioneers of this surgery in Australia . . ." "Pioneer" is defined in the Concise Oxford Dictionary as "the beginner of an enterprise", and the term is quite suitably applied to surgeons who have used a particular technique, though not their own, for the first time in Australia. The article described a stereotactic method with diathermy coagulation which, as Mr. Dowling knows, was first used at the hospital mentioned in my article.

Considering these facts it is evident that the public in Sydney have been well informed that these operations were performed at all major teaching hospitals, long before October, 1959, when my article mentioned that they were also done at the Royal North Shore Hospital.

It is more than surprising to read Mr. Miller's accusations of "blatantly open or thinly veiled advertising" and must be difficult for both the lay and professional reader to draw a conclusion other than that other motives than

the preservation of the "traditional British ethics of our fathers" prompted these letters.

Finally, sir, it is now a generally accepted fact that if medicine and surgery are to advance in New South Wales, then the public must be persuaded to give the research centres a good deal more financial support than it has been wont to do. By far the best medium of instructing the public of their duty in this respect and informing them of how and on what their money is being spent is the public Press.

Yours, etc.,

8 Catherine Street,
St. Ives, N.S.W.
December 11, 1959.

JAMES V. RAMSDEN.

AMBULANCE DRIVERS AND ROAD SAFETY.

SIR: May I write in support of Dr. M. P. Susman's letter (*Journal*, December 19, 1959) which, referring to a fatal accident in which an ambulance was involved, expresses concern at the way these vehicles are driven. I think that most of us would agree that it is only rarely that a patient's outlook will in any way be jeopardized by not "rushing" him to hospital; still less often will the degree of jeopardy outweigh the risks inherent in dangerous driving.

About two years ago I was provoked into writing a letter to the lay Press (under a nom de plume) by a report in *The Sydney Morning Herald* of a trip from Wollongong to Sydney by an ambulance, which was said to have been driven from one city to the other at an average speed of approximately sixty miles per hour. The patient was an injured policeman, who was reported to be suffering from a broken leg. The newspaper recounted this hazardous exploit in terms which implied approval. In addition to regretting the danger to which patient, crew and other road users were exposed by this performance, one could but hope that the broken leg was adequately splinted, and the victim fully sedated.

At the time I suggested that only in cases of asphyxia, serious uncontrolled haemorrhage and poisoning (including bites by snakes or spiders) should ambulance crews assume the responsibility of departing from speed and other road regulations. At present, far from hurrying only in special circumstances, it appears to me that ambulances virtually always speed. In fact, after considering the matter carefully, I cannot recall when I last saw an ambulance being driven without its siren sounding, and at the same speed and in the same manner as other road vehicles; perhaps I have been unobservant, but I do not think so.

None of my remarks is intended as censure of ambulance drivers, whom the public have come to expect to drive fast, and who, admittedly, handle their vehicles with skill; but I am unable to view with equanimity a situation which exposes patients, all road users, and to the greatest degree ambulance crews themselves, to a considerable danger. Surely the subject deserves careful investigation. In how many accidents have ambulance vehicles in this State been involved during the past two years, and with what results? Are Dr. Susman and I correct in our view that speed is rarely justified? Should ambulance drivers be empowered to use sirens only when special circumstances justify a departure from traffic regulations? Should they be required to lodge a report in each such instance? Could the medical profession help ambulance personnel (and probably save the lives of some of them) by laying down guiding principles in the recognition of really urgent cases? Could we hear the views of ambulance authorities on this subject, which is not a simple one? For example, should ambulances speed to a reported accident, even if, as I feel, it is rarely justifiable to hurry once there are patients aboard? What procedure is followed in other States? Could newspapers help by not glamorizing breakneck (I think the word is not inappropriate) dashes by ambulances? Finally, is this not a situation in which the over-riding principle of *primum non nocere* should apply?

Yours, etc.,

225 Macquarie Street,
Sydney.
December 24, 1959.

S. L. SPENCER.

¹ "Premier Congrès International des Sciences Neurologiques, Première Journée Commune", Editions Acta Medica Belgica, 1957.

² *Amer. Geriat. Soc.*, 1956, 12: 14.

³ *Science*, 1947, 106: 349.

⁴ *Arch. Neurol. Psychiat.*, 1954, 71: 598.

⁵ *Arch. Psychiat. Nervenkr., Neurol.*, 1953, 190: 297.

SIR: It is to be hoped that little support will be forthcoming for Dr. M. P. Susman's suggestion that ambulances should not "rush" patients to hospital or sound their sirens.

No doubt in many accident cases the time factor is not important—but surely then the decision could well be left to the ambulance driver. However, that is not true of obstetric problems, cases of poisoning, the obstructed airway, etc.

On the contrary, I feel every effort must be made to educate the police and the public to defer in every way to the speeding ambulance, and to show some appreciation of the well-directed efforts of the magnificent body of men who run this essential ancillary medical service.

Yours, etc.,
"FOR SIRENS."

Newtown.
December 18, 1959.

SIR: As Chairman of the Committee of the Central District Ambulance Service, may I be allowed to comment on the recommendations for which Dr. M. P. Susman asks support in his letter of November 21 last?

1. Drivers of the Central District Ambulance Service are specifically told that, whereas they are expected to attend a call as quickly as possible, they must try at all times to observe traffic rules. It is impressed on them that once a patient is in the ambulance, it is very rarely necessary to hurry.

2. Dr. Susman may know that, in common with police and fire-brigade vehicles, ambulances have certain privileges accorded them by law. Apart from these, the police expect ambulance drivers to obey traffic regulations like any other driver.

3. Contrary to popular belief, ambulance drivers do not enjoy any special dispensation if they do break the law. They are liable to prosecution like any other defaulting driver.

Yours, etc.,
A. W. J. BULTEAU.

19 Beauty Point Road,
Mosman, N.S.W.
December 20, 1959.

A REQUEST.

SIR: I hope some day to make a short monograph on Frederic Wood Jones. In the meantime, I am collecting data on this subject. I would be grateful if any readers of this Journal could assist me with any factual material on this question—e.g., a chronicle, an anecdote, a copy of a letter, etc.

Yours, etc.,
BARRY E. CHRISTOPHERS.

365 Church Street,
Richmond, E.I.,
Victoria.
December 20, 1959.

NONE FOR THE ROAD.

SIR: As a pharmacist, pharmacologist and musician I can give you additional proof of the effect of alcohol on the exercise of skill.

The classical guitar is one of the most difficult instruments to master, and requires skill of the highest degree. I have a very good head for liquor, and feel and appear sober after six fair-sized whiskies. However, I find that after three whiskies my coordination is impaired to such an extent that I fumble an intricate or rapid passage in a piece which normally I can play to perfection.

More than once I have decided not to drive after the guitar had given me its "warning".

Yours, etc.,
"WOULD-BE SEGOVIA."

Rose Bay.
December 18, 1959.

FATAL COLLAPSE DURING EXCHANGE TRANSFUSION.

SIR: I read with interest Dr. S. E. J. Robertson's article in THE MEDICAL JOURNAL OF AUSTRALIA of November 28, 1959. I am surprised that he dismisses the effects of hypercitraemia and hypocalcaemia as a cause of collapse, so readily. I feel also that his evidence that autonomic stress was the cause of death in six cases discussed is very tenuous.

It is recognized that one of the effects of hypercitraemia is spasm in the pulmonary vascular bed and a rise in venous pressure (Firth and Hejhal). Dr. Robertson counteracts this effect by using a negative balance even in the mild cases and, I assume, in those exchanges for hyperbilirubinemia. I have not found this necessary when I have used intravenous calcium in any but the more severely affected cases, i.e., a cord haemoglobin below 10 grammes. Hypocalcaemia undoubtedly plays a part in the symptoms which Dr. Robertson attributes to autonomic stress. The early signs of calcium depletion are restlessness, irritability, excessive salivation and the vomiting of clear mucus. All these effects can be abolished by the administration of intravenous calcium gluconate. I have noticed bradycardia occasionally following this, but it is temporary and not great.

There is a definite relationship between the amount of citrate injected and the ionic calcium depletion; but citrate itself will exert toxic effects in the absence of a low calcium. Citrate is metabolized by most tissues, and especially by the liver. Therefore the rate of removal of citrate is dependent on the situation of the tip of the catheter, i.e., whether in portal circulation or vena cava. It is interesting to note that in Farquhar and Smith's only fatal case there was a hypercitraemia and hypocalcaemia. Dr. Robertson states that shock is more likely in infants of lighter birth weight. This is indeed so, not because of autonomic stress, but because of the direct relationship of birth weight to functional maturity of the liver and consequent citrate removal.

There are obviously other factors involved, such as cooling and hyperpotassaemia. Cooling produces a profound bradycardia, and on one occasion during the depth of winter, the heart rate of one infant I was exchanging dropped to 60 due to inadequate heating. Hyperpotassaemia can also be lethal, but can be avoided by using fresh blood. In Farquhar and Smith's fatal case there was an excess of potassium. Unfortunately, the issue is somewhat clouded in this case due to the presence of a tentorial tear, but it may be that the bleeding was aggravated by the rising venous pressure. Dr. Robertson has obviously evolved on clinical grounds a very efficient and practical way of overcoming his difficulties with citrate by using packed cells and slowing down his rate of exchange. I agree with him that exchanges of a litre per hour with citrated blood are dangerous.

It seems that electrolyte disturbance may cause different pictures according to the electrolyte involved, or the combinations of electrolytes plus such physical factors as cooling, which may also affect electrolyte function. Certainly it would seem advantageous to use heparinized blood where possible as some authors have suggested (Valentine¹, Kelsall²).

Yours, etc.,
N. M. NEWMAN.

71 Davey Street,
Hobart.
December 17, 1959.

GENERAL PHARMACEUTICAL BENEFITS.

SIR: As a member of Council of the New South Wales Branch of the British Medical Association, I have been dismayed by the apparent apathy of the profession towards the Commonwealth Government's proposals to greatly extend the scope of general pharmaceutical benefits to the community. Although these proposals have now been passed by Parliament, the date of implementation is still uncertain because of difficulties still to be ironed out between the Government and the pharmacists. This allows a breathing space for doctors to take a good look at the new Act as it concerns the medical profession, and that is why I address this letter for consideration by the practising doctor throughout Australia, be he specialist or general practitioner.

The Federal Council of the B.M.A. without some real stimulus from the rank and file of the profession has not been able to take any strong stand in this matter, although many of your representatives on various Branch Councils feel very strongly that the new scheme involves real restrictions in prescribing rights immediately and considerable political dangers for the future conduct of medical practice.

¹ Lancet, 1957, 2:1132.

² Arch. Dis. Childh., 1958, 33:142.

³ Lancet, 1958, 2:21.

⁴ Personal communication, 1958.

Has the profession forgotten that in 1948 it won a battle with a previous Government over the right to prescribe freely? That battle was won on legal technicalities which allowed of a case being fought in the courts, but the real objection of the profession was that ordinary prescribing was to be confined to a formulary if the patient was to receive the pharmaceutical benefit. We find ourselves now in virtually the same position; but there has been no hint of a united profession rising in anger to say: "We will not cooperate in this scheme." Does the profession not realize that, as from a date to be declared soon, all prescribing by all doctors for all patients will be technically restricted as to choice of treatment (because the patient will expect a prescription which will qualify for a benefit) and also as to quantities allowable and number of repeats of the prescription?

Those members of the profession who are accustomed to prescribing for pensioners may have become used to the irksome nature of the methods of prescribing for pensioners—the varying decrees as to quantities allowable, number of repeats, number of prescriptions or types of prescriptions on one form (always in duplicate), and the constant changes by additions and deletions of acceptable medicines; but does the member who already prescribes somewhat unhappily for pensioners as a duty towards a needy section of the community accept with equanimity the extension of such restrictions and difficulties to all his patients? And does the doctor who does not at present prescribe for pensioners realize that for all his patients he will have to study the booklet and consider what to prescribe and how much and how often, and how many prescriptions on one form (always in duplicate) every time he prescribes? Sir, is this freedom in prescribing? Does the profession no longer care about restrictions?

Does the average doctor realize how many drugs and prescriptions are unlikely to be among the pharmaceutical benefits anyway? Politicians have a happy knack of suggesting that their handouts will apply to "practically every prescription". If this were so, the profession's case against the scheme would not be so strong; but unfortunately, even at this late stage, your Federal Council has been unable to find out which drugs will be included and which ones excluded from the list of benefits. If the list is to resemble the present pensioner list, as seems likely, the profession should note the virtual absence from it of many common and useful drugs such as antihistamines, antihypertensives, peptic ulcer therapy, arthritis therapy, etc.

In the past the profession has accepted the onus of prescribing two types of pharmaceutical benefit, one being confined to a list which was meant to include only costly drugs which were also life-saving and disease-preventing, and the other a more extended list of drugs for pensioners. We have been happy to cooperate to the best of our ability, although both forms of prescribing imposed difficulties and obligations. It is, however, a far cry from this to what is now proposed, and, be it noted, the profession was not even consulted about the changes, and is not even now allowed to help determine the vastly expanded list of approved prescriptions. Yet we are expected to cooperate in its implementation. Does the profession not realize the future dangers to its freedom once such an extended scheme of pharmaceutical benefits is accepted? No further Acts of Parliament will be needed to add more and more items, or to remove more and more items from the list. In view of the inevitable steep rise in costs of such a scheme in future, it is almost inevitable that a future Government will be compelled to redraft the whole list on the basis that this drug, being cheap, will replace certain others, being dearer, and force on the profession the economic sanction of a restricted formulary based on cost rather than on effectiveness. It is also likely that more and more drugs will be drafted into the section "for specified diseases".

The present Government can have only itself to blame if the rank and file of the profession demand to know the whole scheme in detail, and time for consideration before deciding whether they are willing to cooperate in its implementation. The present situation savours too much of the spider and the fly to be acceptable. I sincerely hope that before the next meeting of the Federal Council, members of the profession in all States of the Commonwealth will let their leaders know to what extent if any they are prepared to cooperate in administering the extended general pharmaceutical benefits scheme.

It would appear that the only reason why this scheme is to be introduced is that the cost of pharmaceutical benefits is constantly rising, coupled with the belief that doctors are forced to choose an expensive "free" drug in

treatment, when a cheaper medicine would do the same amount of good. In my opinion the new scheme will prove infinitely more costly to the taxpayer, while still leaving the same difficulty for the doctor in choosing which drugs to prescribe, while at the same time vastly increasing the number of occasions on which such a choice must be made. Surely the simpler and better alternative would be a careful review of the present limited list of general pharmaceutical benefits, so that it would only contain drugs which are both costly and truly "life-saving" or "disease-preventing".

Yours, etc.,

175 Macquarie Street,
Sydney.
December 18, 1959.

EDWARD S. STUCKEY.

Obituary.

SYDNEY HERBERT ALLEN.

We are indebted to Dr. Colin Macdonald for this appreciation of the late Dr. Sydney Herbert Allen.

The death on September 9, 1959, of Sydney Herbert Allen, in his eighty-third year, severs one of the last remaining links with the Melbourne Medical School of the last century, in the closing years of which Harry Brookes Allen was the Professor of Anatomy. Allen's professorship spanned 42 years, and he exerted an influence on Victorian medicine akin to that of Anderson Stuart in Sydney.

Students then, as now, made their introduction to anatomy and physiology in the second year of the course, and with Allen examining it proved too stiff a hurdle for many at the first attempt; a number of these with sufficient financial backing wasted no time in departing for Edinburgh, where, it was contended, teaching was better. Clinical material was relatively limited in the Scottish capital, and as the competition for students was very keen amongst the many teachers (most of whom lived mainly thereby), the standard of instruction had to be high. There, too, was the added attraction of a medical qualification—in the conjoint licentiate of the Royal College of Physicians and the Royal College of Surgeons—easier to obtain than the M.B. (Melbourne). Many such Australian expatriates did not rest content with the licentiate, but, remaining in Britain for a further two or three years, obtained the higher diplomas (M.R.C.P.E. or F.R.C.S.E.). Almost without exception these young men did very well on returning to Australia, bring with them a *mystique* of having been trained in the Edinburgh school—than which, it was averred by their relatives and friends and patients, there was no better medical school in all Christendom. Most had lived and worked in the storied homeland, across 12,000 miles of ocean, and had acquired a poise and polish and confidence often envied by local graduates. One of these Edinburgh diplomates was Sydney Herbert Allen, F.R.C.S.E.

For hundreds of years the mind of the English-speaking populace has associated characteristics and temperaments of individuals with the nation to which they and their forebears belonged. Everybody knows that the Scots have been linked with financial meanness and love of scholarship, the English with a reserved and phlegmatic temperament allied with caste consciousness, the Irish with the heavy touch of the blarney, and the Jews with flamboyance and aggressiveness. Sydney Allen belonged to the last racial group, but as if to illustrate how erroneous are these time-hallowed misconceptions, nowhere in the world could be found a more modest and self-effacing spirit.

In the eighties and nineties of last century three brothers were very reputable Melbourne bookmakers—Barney (a legendary figure on the Victorian turf), Sam and Benjamin Allen. Benjamin Allen married Julia Goldsmith, and the subject of this memoir, the eldest of their family of four, was born on October 13, 1876, in Drummond Street, Carlton, one of Melbourne's northern suburbs. His matriculation was obtained from the Carlton Grammar School, where the headmaster was Robert Jones. This was one of the private schools—all long since out of existence—which provided secondary education to follow up the primary instruction made free, secular and compulsory by the Victorian Education Act of 1872. Many of those small schools were admirable, inculcating high ethical and spiritual values, and preparing young people for effective future citizenship and the realities of community life; but they were doomed with the growth of the large and powerful church and high

schools, and today they and their work are remembered by only a few elderly antiquarians.

Allen had spent two years in the medical course at Melbourne, later becoming a Licentiate of the Royal College of Surgeons of Edinburgh, in 1900; after some years as a houseman in British hospitals, he gained the Fellowship of the Royal College of Surgeons of Edinburgh in 1903; 26 years later he was elected a foundation Fellow of the Royal Australasian College of Surgeons.

In Edinburgh, the two men who most influenced Allen were Alexis Thomson and Halliday Croom. Thomson had a decisive and epigrammatic style, found very stimulating by his students. At a later period (in 1904) he became Professor of Surgery, and in collaboration with Alexander Miles

General Hospital in *Orontes* for Egypt, later to proceed to France; my late partner, Sir Stanley Argyle, often told me how happy a band of medical officers were those in *Orontes*. Allen was demobilized in 1918, and returned to his Carlton practice. Later he practised at St. Kilda, where he was City Health Officer for a period of 17 years that terminated only a few weeks before his death.

Resident medical officers at the Women's Hospital were always pleased when allotted to Allen's beds, for if they won his approval by keeping good histories and treating patients with humanity and kindness, he was very generous with operations performed under his guidance; this obtained particularly in his latter years, when he suffered from frequent bouts of crippling lumbago; he would sit beside the operating table quietly giving instructions and encouragement.

Allen did very little systematic teaching, either at the bedside or in the lecture room; nor do I recall any contribution by him to medical literature. I had an occasion many years ago to discuss with Syd his teaching inactivity. "I realize my apparent shortcoming in this regard", he reflected in his slow, husky voice, "but I believe that unless those asked to teach have a gift of exposition, it is better for the students to do most of their work themselves. There are now excellent textbooks available, and I have the feeling they are being subjected to a hyperalimentation in lectures and demonstrations, which occupy practically every hour of their day; many have no time to stand and stare, to play a game of football or even billiards. I feel that I can fulfil the best function by helping and encouraging my stream of residents to perform, skilfully and with confidence, those gynaecological operations they may be called upon to undertake in general practice, perhaps many miles from a surgical centre. I believe it is because of this surgical opportunity—limited though it may be—that in the past, at least, our Australian general practitioners have acquired a world-wide reputation for all-round competence superior to those of many other countries."

Allen was of average height and build, always immaculately dressed (bowler hat, gloves and cane matching), with the features of his forebears, and dark eyes always twinkling with kindness; he had no enemies and he spoke no ill of anyone. Allen loved sociable company, and was a devoted member of the University Club, being its president for no fewer than 33 years. Here he could always be certain of a keen hand of bridge or poker or billiards; here, too, he would be kept up to date on the acceptances or starting prices for Flemington, Caulfield, Moonee Valley or even the Ballarat Miners. The University Club of Melbourne, first founded in 1903, has never enjoyed the strong support of its counterpart in Sydney; but Allen was very proud that amongst his predecessors as its president were men of the eminence of Sir John Madden, Sir Leo Cussen and Sir John Monash. Allen was a lifelong devotee of horse racing, and was honorary surgeon to the Moonee Valley Racing Club for 35 years; in spite of reputedly the best of information, combined with an unquenchable optimism, he won no fortune from the turf.

He married Miss Eileen O'Connell, of Melbourne, who predeceased him by some years; a son, Mr. Sydney Hilary Allen, the only child, survives.

There appears to be little place today for Sydney Allen's methods of passing on the surgical torch. They are as dead as the dodo; yet there are some who believe that our profession is the poorer. Allen was a kind and generous spirit, whose name the Royal Women's Hospital, Melbourne, is proud to have included in its "Book of Remembrance".



published "A Manual of Surgery" and "A Manual of Operative Surgery", which established themselves as standard textbooks in Britain and abroad. For almost 50 years Halliday Croom was celebrated as a lecturer, taking infinite trouble to prepare every lecture he delivered, and during his time as an extramural lecturer at Edinburgh, no student's course was considered complete unless he had attended Croom, appointed University Professor of Midwifery in 1905.

On returning to Melbourne, Allen succeeded to the general practice of John Gordon, when the latter was appointed In-Patient Surgeon to the Melbourne Hospital. During this period he worked hard at public charities, for he held the positions of the first Medical Superintendent at the Infectious Disease Hospital at Fairfield (to which he drove daily in his shining black jinker), Surgeon to Out-Patients at the Children's Hospital, and Anaesthetist at St. Vincent's Hospital. The Matron at Fairfield in Allen's day was Miss Evelyn Conyers, later Matron-in-Chief of the Australian Nursing Services in the first World War. Allen was appointed Out-Patients' Surgeon at the Women's Hospital in 1914, in the same year as his friends Edward White, Arthur Sherwin, William Cusack, Lennox Speirs and Milne Sutherland; of this distinguished band only Sherwin and Speirs remain. The leaders at the Hospital then were Felix Meyer, Reginald Morrison and F. W. W. Morton. This was the year of the outbreak of the first World War, and twelve months later Allen sailed with the second Australian

Naval, Military and Air Force.

APPOINTMENTS.

THE following appointments, changes etc. are published in the *Commonwealth of Australia Gazette*, No. 69, of November 5, 1959.

ROYAL AUSTRALIAN AIR FORCE.

Permanent Air Force.

Medical Branch.

The probationary appointment of the following Flight Lieutenants is confirmed:—D. P. Adamson, M.B.E. (0310768), E. B. Morgan (0310769), P. A. Mead (0310771), D. C. Mintz (0310772), C. T. Flynn (0310773), R. J. Smith (0310774).

The surname in the notification regarding the appointment to a commission of Kenneth William Pritchard (055804) as approved in Executive Council Minute No. 24 of 1959, appearing in Gazette No. 50 dated 13th August, 1959, is amended to read, Prichard.

Air Force Reserve.

Medical Branch.

Kurt Singer (295571) is appointed to a commission, 30th September, 1959, with the rank of Flight Lieutenant.

Michael Guerin (043099) is provisionally appointed to a commission, 8th September, 1959, with the rank of Pilot Officer.

The following appointments, changes etc. are published in the *Commonwealth of Australia Gazette*, Nos. 71 and 72, of November 12 and 19, 1959.

AUSTRALIAN MILITARY FORCES.

Australian Regular Army.

Royal Australian Army Medical Corps (Medical).

To be Temporary Major, 21st September, 1959.—3/40147 Captain R. H. Meyer.

Citizen Military Forces.

Northern Command.

Royal Australian Army Medical Corps (Medical).—To be Temporary Major, 1st October, 1959.—1/59814 Captain (provisionally) B. E. Todd.

Eastern Command.

Royal Australian Army Medical Corps (Medical).—The provisional appointment of 2/142616 Captain J. J. Waddell is terminated, 31st July, 1958. To be Captain (provisionally), 1st August, 1958.—2/142616 John James Waddell.

Central Command.

Royal Australian Army Medical Corps (Medical).—4/35233 Lieutenant-Colonel J. D. Rice is appointed to command 104th Military Hospital and to be Colonel, 1st October, 1959. 4/31901 Colonel R. G. C. De Crespigny, E.D., relinquishes command 104th Military Hospital, 30th September, 1959, and is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Central Command), 1st October, 1959. 4/31903 Lieutenant-Colonel C. M. Gurner relinquishes command 1st Casualty Clearing Station, 30th September, 1959.

Western Command.

Royal Australian Army Medical Corps (Medical).—The provisional appointment of 5/26529 Captain M. Traub is terminated, 29th September, 1959. To be Captain (provisionally), 30th September, 1959.—5/26529 Max Traub.

Tasmania Command.

Royal Australian Army Medical Corps (Medical).—2/127012 Major T. W. Horne is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Tasmania Command), 1st September, 1959.

Reserve Citizen Military Forces.

Royal Australian Army Medical Corps (Medical).

The following officers are retired, 31st October, 1959:—

Northern Command.—Honorary Captain J. V. Guinane.

Southern Command.—Honorary Captain M. H. Troup.

The following officers are placed upon the Retired List with permission to retain their rank and wear the prescribed uniform, 31st October, 1959.

Northern Command.—Captain D. P. H. Schafer.

Southern Command.—Captain F. J. Bryan.

NAVAL FORCES OF THE COMMONWEALTH.

Citizen Naval Forces of the Commonwealth.

Royal Australian Naval Reserve.

Promotions.—Surgeon-Lieutenant Alastair Charles Cole is promoted to the rank of Surgeon Lieutenant-Commander, dated 21st August, 1959.

Royal Australian Naval Volunteer Reserve.

Appointments.—Surgeon Lieutenant-Commander Arthur George Harrold, Royal Australian Naval Reserve, is appointed Surgeon Lieutenant-Commander, with seniority in rank of 29th November, 1953, dated 12th October, 1959.

The following appointments, changes etc. are published in the *Commonwealth of Australia Gazette*, No. 81, of December 17, 1959.

ROYAL AUSTRALIAN AIR FORCE.

Permanent Air Force.

Medical Branch.

Malcolm John Hoare (0310780) is appointed to a short-service commission on probation for a period of twelve months, 16th September, 1959, with the rank of Flight Lieutenant.

Squadron Leader A. Cameron (039928) is granted the acting rank of Wing Commander, 1st November, 1959.

Flight Lieutenant D. P. Adamson, M.B.E. (0310768) is appointed to a permanent commission, 1st September, 1959.

Active Citizen Air Force.

Medical Branch.

No. 24 (City of Adelaide) Squadron.—Flight Lieutenant D. S. Forbes (042994) is transferred to the Reserve, 17th October, 1959.

Air Force Reserve.

Medical Branch.

The provisional appointment of Pilot Officer G. S. Baron-Hay (053080) is confirmed and he is promoted to the rank of Flight Lieutenant, 30th September, 1959.

The appointment of the following officers is terminated, 1st October, 1959: Flight Lieutenants (temporary Squadron Leader) R. W. Greville (257932); Flight Lieutenants A. Bardsley (257498), J. B. Cahill (263188), R. G. Cameron (036604), P. F. Claremont (024267), D. Lenaghan (257916), G. B. Markey (04706), J. F. Marrington (021966), L. J. Ray (253941), J. G. H. Refshauge (409447), K. M. Twiddy (419145), F. X. M. Willis (438633); Pilot Officers I. D. Cameron (024311), G. J. Long (0212338).

Notes and News.

"Human Factors."

A new journal has been produced by the Human Factors Society of America with the title *Human Factors*. In the study on which this journal is based, the human factor is considered in relation to the machines and environments in which man works and plays. This is an important topical subject, about which a good deal has been thought and much has been written. The new journal will provide a means for the reporting of studies in this field and a forum for discussion of the problems involved. The subscription rate is £310s. (sterling) per annum for a total of four issues. It is available from the Pergamon Press Limited, 4-5 Fitzroy Square, London, W.1.

Evan Jones Memorial Prize, 1960.

The following information relating to the Evan Jones Memorial Prize has been received from the Australasian Association of Psychiatrists.

A prize to the value of £50 shall be awarded triennially to the candidate who, in the opinion of the examiners, has made the most substantial contribution to knowledge in the subject of psychiatry, or in a field closely related thereto, during the three years prior to the award.

The recipient must be a registered medical practitioner practising his profession in Australia or New Zealand.

The material submitted for the prize may be either a thesis or one or more published works in medical or scientific literature. The entry shall be suitably bound.

Each candidate must declare that the work described is his own.

Four typed or printed copies of the entry shall be submitted to The Honorary Secretary, Australasian Association of Psychiatrists, 34 Erin Street, Richmond, Victoria, and marked "Evan Jones Memorial Prize".

The closing date for the present competition will be September 1, 1960.

The prize shall not be awarded on any occasion unless in the opinion of the examiners the material submitted is of sufficient merit.

The successful contribution shall remain the property of the Association.

A New Journal of Psychosomatic Medicine.

We have received the first number of a new French journal with the title *Revue de médecine psychosomatique*. It is to be a quarterly journal, the first issue covering the period January to March, 1959; in it will be published original articles and other material relating to psychosomatic medicine. The annual subscription is 2300 francs. Inquiries should be directed to Les Editions de Médecine Pratique, 12, rue Pierre-Geofroix, Colombes (Seine), France.

Q.T. Australia.

It is reported for the information of the medical profession in South Australia that there has now been formed a South Australian branch of Q.T. Australia. As is well known, this organization, originally formed in New York, is for people who have undergone ileostomy for ulcerative colitis. It is the intention of the branch to meet every two months for discussions of ileostomy problems and other matters of mutual interest, and members of the medical profession are invited to attend these meetings. Members of the organization will also be available for hospital visiting at the request of surgeons. The meetings will be held at the Estonian Hall, 200 Jeffcott Street, North Adelaide, on the first Thursday in each even month, commencing on Thursday, February 3, 1960, at 8 p.m. Further information may be obtained from the honorary secretary, Mr. W. R. S. Wallis, 32 Warwick Avenue, Kurralta Park (Telephone LF 2097), who will also be pleased to arrange hospital visiting.

"Epilepsia."

The International League against Epilepsy has decided to produce its official organ, *Epilepsia*, as a quarterly journal. The first number, dated March, 1959, in this

fourth series has now been received. With Sir Francis Walshe as editor-in-chief, it is an attractive publication which should be widely acceptable. The object has been to provide a journal in which will be found informed, original and critical studies on epilepsy from the point of view of aetiology, pathogenesis, course, manifestations, investigations of a relevant kind, and treatment both medical and surgical. It is hoped to encourage studies in the morbid anatomy of the epileptic brain and to provide a journal for all who, from any aspect or by any relevant method of study, seek to advance the study of epileptic manifestations, whether they work as clinicians, surgeons, electrophysiologists, biochemists or physical chemists. This new journal is published by the Elsevier Publishing Company, Amsterdam, but the distributors in the British Commonwealth are the D. Van Nostrand Company Limited, 358 Kensington High Street, London, W.14. The subscription rate is £215s. (sterling) per volume of four issues.

Post-Graduate Work.

SEMINARS AT ST. VINCENT'S HOSPITAL, SYDNEY.

A SERIES of medical seminars will be held at St. Vincent's hospital, Sydney, on the second and fourth Tuesdays of each month, commencing on February 9. On the first and third Tuesdays an interesting medical case will be presented. These sessions will commence at 1.15 p.m. and continue until 2 p.m. Luncheon will be served at 12.45 p.m. The programme is as follows:

February 9: "Pharmacological Research in the Cardiac Field", Professor R. H. Thorp, Professor of Pharmacology, University of Sydney.

February 23: "Renal Arteriography", Dr. G. Benness.

March 8: "Some Aspects of Calcium Metabolism", Dr. L. Watson, Senior Lecturer in Medicine, University of Sydney.

March 22: "The Spastic Colon", Dr. B. P. Billington, Assistant Physician, Sydney Hospital.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED DECEMBER 12, 1959.¹

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	3	3(3)	6
Amoebiasis
Ancylostomiasis	3	4	..	7
Anthrax
Bilharziasis
Brucellosis	2	2
Cholera
Chorea (St. Vitus)
Dengue
Diarrhoea (Infantile)	11(6)	6(6)	4(3)	1(1)	1(1)	..	3	..	26
Diphtheria	1(1)	1
Dysentery (Bacillary)	4(2)	1	..	5
Encephalitis	1(1)	1
Filariasis
Homologous Serum Jaundice
Hydatid
Infective Hepatitis	61(22)	45(32)	13	14(6)	6(3)	2	141
Lead Poisoning	2	..	2
Leprosy	2	2
Leptospirosis	1	..	1
Malaria	1	4
Meningococcal Infection	1	2(2)
Ophthalmia
Ornithosis
Paratyphoid
Plague
Poliovirus	2(2)	2
Puerperal Fever	1	1
Rubella	24(20)	4(3)	4	32
Salmonella Infection	5(5)	3(1)	8
Scarlet Fever	2(1)	19(17)	5(4)	5(3)	1	32
Smallpox
Tetanus	1(1)	1
Trachoma	1	..	29	..	30
Trichinosis
Tuberculosis	23(15)	21(13)	13(7)	2(1)	7(3)	3(1)	..	1	70
Typhoid Fever	3(3)	3
Typhus (Flea-, Mite- and Tick-borne)	1	1
Typhus (Louse-borne)
Yellow Fever

¹ Figures in parentheses are those for the metropolitan area.

April 12: "Diuretics", Professor R. Blacket, Professor of Medicine, University of New South Wales.

April 26: "Primary Pulmonary Hypertension", Dr. M. Farrar, Research Fellow, Cardiac Department, Royal Alexandra Hospital for Children.

May 10: "The Lungs in Heart Disease", Professor J. McMichael, Professor of Medicine, Postgraduate Medical School, London.

May 24: No seminar.

June 14: "Clinical Problems in Blood Coagulation", Dr. P. Lamond.

June 28: "Acute Fulminating Pneumonia", Dr. J. Benecke.

July 12: "The Treatment of Severe Hypertension", Dr. G. Bauer, Assistant Physician, Sydney Hospital.

July 26: "Cushing's Syndrome", Dr. J. Hickie.

August 9: "Bronchitis", Dr. A. G. McManis.

August 23: "Physical Principles in the Cardio-Vascular System", Dr. P. George.

September 13: "Chlorpromazine Jaundice", Dr. P. O'Brien.

September 27: No seminar.

October 11: No seminar.

October 25: "The Porphyrias", Dr. D. Rothfield.

November 8: "Diabetic Coma", Dr. L. Lazarus.

November 22: "Neuropathies due to Alcohol", Dr. J. Allsop, Assistant Physician, Royal Prince Alfred Hospital, and Dr. B. Turner, Neuro-Pathologist, Division of Psychiatric Services.

December 13: "The Long-Term Sequelæ of Radiotherapy", Dr. L. Atkinson.

Corrigendum.

RADIOLOGY ABSTRACTS.

IN the radiology abstracts in the issue of December 26, 1959, under the heading "Cystic Disease of the Renal Pyramids", the reference to the paper concerned is incorrectly quoted as from the *British Journal of Radiology* for July, 1959; the paper actually appeared in the *Journal of the Faculty of Radiologists* for July, 1959. We apologize for this error.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Sinclair, Agnes Esther, M.B., B.S., 1958 (Univ. Sydney), 45 Barker Road, Strathfield.

Munster, Andrew Michael, M.B., B.S., 1959 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Knott, Bernays Melville, M.B., B.S., 1958 (Univ. Sydney), 9 Allawah Place, Greenwich.

Pritchard, Elizabeth, M.B., B.S., 1958 (Univ. Sydney), 150 Penshurst Street, Willoughby.

Jeremy, Ross, M.B., B.S., 1957 (Univ. Sydney), 10 Wesley Street, Greenacre.

Medical Appointments.

THE undermentioned appointments have been made to the Honorary Medical Staff of the Royal Alexandra Hospital for Children.

Dr. F. Fisher, Dr. H. F. F. Lorang and Dr. J. N. Nicholas have been appointed Honorary Anaesthetists.

Dr. G. S. Colvin and Dr. C. M. Maxwell have been appointed Honorary Orthopaedic Surgeons.

Dr. R. W. D. Middleton and Dr. D. W. Whiteway have been appointed Honorary Assistant Orthopaedic Surgeons.

Deaths.

THE following deaths have been announced:

HOWELL.—David Leslie Howell, on December 28, 1959, at Wangi Wangi, New South Wales.

HARRIES.—John Victor Harries, on January 1, 1960, at Hobart, Tasmania.

Diary for the Month.

JANUARY 18.—Victorian Branch, B.M.A.: Finance, House and Library Subcommittee.

JANUARY 19.—New South Wales Branch, B.M.A.: Executive and Finance Committee.

JANUARY 21.—Victorian Branch, B.M.A.: Executive of the Branch Council.

JANUARY 22.—Queensland Branch, B.M.A.: Council Meeting.

JANUARY 26.—New South Wales Branch, B.M.A.: Medical Politics Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

Authors of papers are asked to state for inclusion in the title their principal qualifications as well as their relevant appointment and/or the unit, hospital or department from which the paper comes.

References to articles and books should be carefully checked. In a reference to an article in a journal the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this Journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in Australia can become subscribers to the Journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £6 per annum within Australia and the British Commonwealth of Nations, and £7 10s. per annum within America and foreign countries, payable in advance.